Exploring the practises and effects of gluten-free and low FODMAP diets in noncoeliac athletes

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Dissertation submitted in fulfilment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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February 21, 2017

UNIVERSITY of TASMANIA

Declarations

Declaration of Originality

I hereby declare that this thesis entitled "Exploring the practises and effects of gluten-free and low FODMAP diets in noncoeliac athletes" contains no material which has been accepted for a degree or diploma by the University of Tasmania or any other institution, except by way of background information and duly acknowledged in the thesis, and to the best of my knowledge and belief no material has previously been published or was written by another person except where due reference is made in the text of the thesis, nor does the thesis contain any material that infringes Copyright Act 1968.

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- Located in Chapter 2
- Candidate was the primary author, and with authors 1 and 4, contributed to the conceptualization of the research design and all authors contributing to the drafts of the manuscript.
- The candidate developed and implemented the questionnaire tool with input from authors 1, 3 and 4.
- The candidate conducted all data analysis with significant contribution from author 4.

Paper 2: No effects of a short-term gluten-free diet on performance in noncoeliac athletes

- Located in Chapter 3
- Candidate was the primary author contributed to 80% of the planning and execution of the research project and subsequent publication.
- Authors 1, 3 and 4 contributed to the conceptualization of the research design.
- Authors 1, 2 and 3 contributed significantly to execution of laboratory trails and analysis.
- Author 2 contributed significantly to data interpretation and analysis.
- All authors contributing to the drafts of the manuscript.

Paper 3: Food avoidance in athletes: FODMAP foods on the list

- Located in Chapter 4
- Candidate was the primary author and contributed 90% to the concept, analysis and interpretation of this manuscript.
- All authors contributed to drafts of the manuscript.
- Author 2 contributed significantly to data interpretation, analysis and manuscript revision.

Paper 4: Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms

- Located in Chapter 5
- Candidate was the primary author and contributed 85% to the conceptualization, planning and execution of this study.
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Paper 5: Commercial Hype Versus Reality: Our Current Scientific Understanding of Gluten and Athletic Performance.

- Located in Chapter 7
- Candidate was the primary author and contributed to 90% of writing of this manuscript.
- Author 2 and 4 contributed significantly to the manuscript revisions

Paper 6: A preliminary study of FODMAP modulation as a novel strategy to reduce gastrointestinal distress in athletes

- Located in Chapter 6
- Candidate was the primary author contributed to 90% of the planning and execution of the research project and subsequent publication.
- All authors contributed to the conceptualization of the research design and drafts of the manuscript.
- Author 2 contributed significantly to data interpretation and analysis.

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Statement of Contribution to Thesis

The thesis comprises four research investigations which have been completed almost entirely by the candidate, Dana Lis. Dana Lis (School of Health Sciences, University of Tasmania): Study design, lead role in recruitment, data collection, data analysis and interpretation, first author on all manuscripts (Chapters 2 to 7). However, the following people also contributed to each of the studies as detailed:

- James Fell (School of Health Sciences, University of Tasmania): Advised on study design, assisted with data collection (blood collection, exercise testing), statistical analysis, manuscript revisions.
- Kiran Ahuja (School of Health Sciences, University of Tasmania): Study design, data collection (blood collection) and management, statistical analysis (planning and completing), data interpretation, manuscript revisions.
- Trent Stellingwerff (Canadian Sport Institute Pacific, University of Victoria, Victoria, British Columbia, Canada): Advised on study design, recruitment, data presentation, manuscript revisions.
- Cecilia Kitic (School of Health Sciences, University of Tasmania): Advised on study design, assisted with data collection and analysis (blood collection, exercise testing), manuscript revisions.

Additional support was contributed from the following students on certain aspects of the thesis projects, as follows:

- Emma Smith (School of Health Sciences, University of Tasmania): Assisted with recruitment, study logistics and exercise testing for an undergraduate project which was completed on results from a small sample of participants in this study.
- Isabelle Goodwin (School of Health Sciences, University of Tasmania): Assisted with data entry and study logistics for study 4.

- Sarah Webber (University of Colorado, Colorado Springs, USA): Assisted with data entry as part of her Sport Nutrition practicum experience.

Statement of Ethical Conduct

- The research associated with this thesis abides by the international and Australian codes of human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University (Tasmania) Network: (Approval numbers: H0015151, H0013244 and H0015151).

Dana M. Lis Date: February 21, 2017

List of Publications

Lis D, Stellingwerff T, Shing CM, Ahuja K, DK, Fell J. Exploring the popularity, experiences, and beliefs surrounding gluten-free diets in noncoeliac athletes. *Int J Sport Nutr Exerc Metab.* 2015; 25:37-45.

Lis D, Stellingwerff T, Kitic CM, Ahuja KD, Fell J. No effects of a short-term gluten-free diet on performance in noncoeliac athletes. *Med Sci Sports Exerc.* 2015; 47(12):2563-70.

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Food avoidance in athletes: FODMAP foods on the list. *Appl Physiol Nutr Metab.* 2016;41(9):1002-4.

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms. *Int J Sport Nutr Exerc Metab.* 2016. 26(5): 481-7.

Lis DM, Fell JW, Ahuja KD, Kitic CM, Stellingwerff T. Commercial hype versus Reality: Our current scientific understanding of gluten and athletic performance. *Curr Sports Med Rep.* 2016;15(4):262-8.

Conference Presentations

October 2013: **Sports Dietitians of Australia Conference** (Melbourne, Australia), Poster: *Gluten-free diet questionnaire study overview and presentation of results.*

October 2013: **Sports Medicine Australia** (Phuket, Thailand), Poster: *Athletes and gluten-free diets: Exploring the popularly, experiences and beliefs of this diet in non-coeliac athletes.*

October 2015: **Sports Medicine Australia Conference** (Gold Coast, Australia), Oral: *No effect of gluten-free diets on performance, gastrointestinal health or wellbeing in non-coeliac endurance athletes.*

October 2015: **Sports Dietitians of Australia Conference** (Melbourne, Australia), Oral: *No effects of a short-term gluten-free diet on performance in noncoeliac athletes.*

May 2015: **American College of Sports Medicine Annual Meeting** (San Diego, CA, United States of America), Poster: *The effects of gluten-free diets on performance, gastrointestinal symptoms, inflammation and perceptual wellbeing in noncoeliac athletes.*

May 2016: **American College of Sports Medicine Annual Meeting** (Boston, MA, United States of America), Oral: *Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms.*

October 2016: **Canadian Society for Exercise Physiology** (Victoria BC, Canada), Poster: *From gluten to FODMAPs: Dietary strategies to combat gastrointestinal symptoms in athletes.*

October 2016: **Sports Medicine Australia** (Melbourne, VIC, Australia), Oral: *Case Study: Utilizing A low FODMAP diet to combat exercise-induced gastrointestinal symptoms.*

November 2016: **Sport Innovation Summit** (Calgary, AB, Canada), Oral: *Commercial hype versus reality: Our current scientific understanding of gluten-free diets and athletic performance.*

Funding Support, Awards and Grants

Canadian Sport Institute Pacific Research and Innovation funding support, 2013

Judith Homeshaw Scholarship for Women's Involvement in Science, 2013

Sport Dietitians Australia Research Grant, 2013

Sports Medicine Australia Research Grant, 2013

King and Amy O'Malley Trust Scholarship, 2013 (3-year)

University of Tasmania International Travel Grant to attend the American College of Sports Medicine Annual Meeting, 2015

Food product donation from the Manildra Group, Orgran, PureBred and Brookfarm for study food.

Acknowledgements

Foremost, I would like to thank and acknowledge the support of my supervisors; Dr James Fell, Dr Kiran Ahuja, and Dr Cecilia Kitic and Dr Trent Stellingwerff for their unwavering support, mentorship, patience, friendship and guidance through the journey of this thesis. Dr Fell was a pillar of support from day one and taught me the ropes of academia, improved my physiology knowledge and always brought comic relief to when stress levels were elevated. We both operate in grey areas and prefer asking for forgiveness after the fact, so we were a good team. Dr Ahuja's attention to detail and commitment to devoting time to consider diverse aspects of analysis pushed me to strive for excellence which was key for the many successes of this research. Dr Kitic was by my side to mentor my laboratory skills and writing throughout this entire journey as we both became new mothers. Her kindness, patience and confidence in me pushed me to get the most out of my academic journey. Dr Stellingwerff has been a career and academic mentor for over 8 years. His communication skills, expansive knowledge, optimism and methodical approach to problem solving has taught me what it takes to be a world class sport science practitioner, mentor and academic; simultaneously (unfortunately I am lacking the photographic memory part). Sincere thanks to Emma Smith, Isabelle Goodwin and Sarah Webber for their support with study logistics and data entry. Sincere gratitude is extended to Steve Stone for being the best lab guru ever (and not a bad cyclist either) and Emma Zadow for unwavering willingness to train my laboratory skills, physiology knowledge and being a genuine friend.

I am grateful to the Judith Homeshaw fund and King and Amy O'Malley Trust for financial support, the School of Health Sciences, University of Tasmania for providing additional funding to undertake my studies and the Canadian Sport Center Pacific for their financial and personnel investment in this research.

Deepest gratitude goes to my study participants who kindly gave me so much time and tolerance; this thesis would not have been possible without you. Thanks to my fellow PhD and Masters candidates for embracing a baby/toddler in the work space/lab, even babysitting sometimes, enjoying morning tea and always offering a laugh.

A very special thank you to my parents, Mark and Cynthia who dropped everything many times over the past 4 years to fly across the world to help a me, as a new mum, balance work, study and the most precious little person. My baby Myles, who has grown into a little boy since this journey began, for his contagious smiles, hugs, hilarity, insightfulness and overwhelming amazingness. From being relatively close to being born in the lab to being able to verbalize "are you done with your thesis" having Myles along throughout this journey always put everything into context and even the worst reviewer comments are just a problem to be solved, rather than a catastrophe. Last, but certainly not least, my incredible husband, Alex: the greatest mentor, supporter and Fireball aficionado of all time. Pursuit of a PhD would not even have been considered without his drive for excellence, giant brain and relentless belief in me. Alex has been my rock for almost 20 years and his unwavering support has pushed me to get the most out of every day. We continue to push each other to strive for excellence while enjoying every moment and cherishing our family. This PhD journey has been great, but more than anything I am looking forward to turning my attention 110% back to my family with the weight of this endeavour lifted. From the bottom of my heart, thank you to every special individual who has given part of themselves to mentor me along this journey.

General Abstract

Background and Aims

Exercise-associated gastrointestinal (GI) symptoms are widespread and estimated to occur in 30-50% of endurance athletes. GI symptoms are multi-factorial but primarily caused by physiological, mechanical and/or nutritional triggers. Symptoms generally occur during exercise or within the few hours following exercise. Gluten is touted by many to be detrimental to GI health in athletes particularly with a compromised gut barrier caused by reduced splanchnic blood flow, which most commonly occurs during higher exercise intensities. It is suggested that exercise-induced injury to the gut barrier could in turn increase susceptibility to dietary triggers, such as gluten. Gluten is further perceived to elicit undesirable pro-inflammatory responses in healthy athletes, partially through compromised gut epithelial barrier function, allowing the passage of gluten peptides or the interaction of these peptides with tight junction proteins. However, these theories alongside the overall idea that a gluten-free diet (GFD) provides an ergogenic benefit have yet to be substantiated.

Athletes persistently explore dietary strategies perceived to offer ergogenic benefits or beneficial impacts on parameters influencing performance, such as reducing GI symptoms. There has been an explosion in the prevalence and use of gluten-free products in recent years, which is exacerbated by unsubstantiated commercial health and sport performance claims. This has led to numerous athletes touting a gluten-free lifestyle as the secret to their success. It is well known that a GFD is necessary for the treatment of clinical conditions such as coeliac disease or noncoeliac gluten (wheat) sensitivity (NCGS). However, anecdotal reports suggest that many athletes believe a GFD directly improves exercise performance and parameters influencing performance, particularly GI symptoms as well as inflammation and immune

health.

Dietary changes may occur alongside the avoidance of gluten-containing foods that could influence health parameters or GI symptoms. A predominant dietary change that occurs subsequent to eating a GFD also includes a reduction in the intake of short-chain carbohydrates, otherwise known as fermentable, oligo-, di-, monosaccharides and polyols (FODMAPs). Significant FODMAP reduction may actually modulate GI symptoms, and not necessarily the gluten itself. Given the absence of peer-reviewed data on the effects of either gluten or FODMAPs on athlete performance, the studies that comprise this thesis were first aimed to understand and quantify the prevalence of GFD adherence, and relatedly, high FODMAP food avoidance among noncoeliac athletes (NCA). A second step was to undertake intervention studies to investigate the efficacy of these diets on GI symptoms, performance and related parameters in an athletic population.

Methods and Results

An electronic-based questionnaire (n=910) was distributed internationally to athletes to determine athlete-specific GFD and high FODMAP avoidance food behaviours and beliefs. Specifically, this questionnaire was designed to evaluate GFD practises, demographics, experiences, and sources of dietary recommendation and information. Our initial findings established that 41% of NCAs followed a GFD at least 50% of the time. Negative GI symptoms (e.g. diarrhoea, bloating) were the most highly reported indicators believed to be triggered by gluten with 84% of respondents indicating symptom improvement with gluten-removal. Athletes adhering to a GFD also perceived a GFD to improve body composition for sport (74.4%), reduce inflammation (73.3%), decrease GI distress (61.1%), and improve exercise performance (56.3%). Self-diagnosed gluten-related conditions were the primary reason for

adopting a GFD with non-medical dietary prescription and advice from coaches/other athletes reported as the most common source of GFD information.

Given the high uptake of a GFD in athletes and the belief that a GFD improved exercise performance, GI health and wellbeing, the next study within this thesis aimed to investigate the effects of a GFD on performance in endurance-based NCA. Thirteen competitive NCA (endurance cyclists) were allocated to a 7-day gluten-containing diet (GCD) or GFD (16 g gluten.day^{-1}) using a controlled, double-blind, crossover intervention design. During each diet, cyclists completed GI questionnaires (daily and during exercise), the Daily Analysis of Life Demand for Athletes (DALDA) and an exercise test on day seven of each dietary period. Blood samples were taken pre-exercise, after a 45-minute steady state exercise bout at 70% W_{max} and following a 15-minute time trial (TT) to measure acute intestinal injury and inflammatory markers. Exercise and dietary intake was tightly controlled and replicated during each dietary period. A GFD had no beneficial or negative effect on 15-minute cycling TT performance (GCD 245±53 and GFD 245±55 kJ). GI symptoms, DALDA evaluation and biomarkers of acute epithelial injury and systemic inflammation were also similar in the GCD and GFD periods.

The GFD intervention did not show a GFD to be ergogenic; however, when a GFD is adopted, FODMAPs may be reduced. The low rates of GI symptoms reported in our initial study may have been confounded by a reduction in fructans on both trials, which are part of the FODMAPs family. Initial findings led to subsequent studies investigating FODMAP avoidance or reduction in NCA. First, athletes' dietary behaviours regarding FODMAPs were established via FODMAP-specific questions in the preliminary questionnaire-based study. Offending foods that happened to be part of the FODMAP family were quantified as a popular strategy employed by 51% of NCA to reduce GI symptoms with 83% of this group reporting symptom

improvement. To examine the effects of short-chain carbohydrate restriction on GI symptoms, a short-term low FODMAP dietary intervention was conducted utilizing a case-study methodology in a multisport athlete with persistent exercise-associated GI distress. A 6-day low FODMAP compared to a habitual high FODMAP diet was implemented and the athlete was evaluated for GI symptoms and DALDA scores indicating 'worse than normal.' On each day of the intervention a measurable reduction, from symptom severity scores of 0-9 to 0, in exercise and daily GI symptoms was observed. DALDA scores remained stable across the habitual and intervention periods. The GI symptom improvement in this athlete suggested the necessity for a larger crossover intervention to further explore the use of a FODMAP restricted diet as a tool to reduce GI distress in healthy symptomatic endurance athletes.

To further explore the potential of a low FODMAPs intervention to reduce GI symptoms, a larger preliminary trial was conducted. GI symptoms and perceptual wellbeing were assessed during a high FODMAP vs. low FODMAP diet in runners (n=11) with persistent exercise-associated GI symptoms, but no diagnosed functional gastrointestinal disorder or food intolerance. Runners were randomized to low (<9 g FODMAP.day^{-1}) and high FODMAP (>20 g FODMAP.day^{-1}) dietary periods of 6-days each with prescribed strenuous running sessions completed on day-4 and day-5 and a single day washout before crossing over to the other diet. Exercise and diet were replicated with study meals and snacks provided alongside suitable low or high FODMAP food choices. During each dietary trial runners recorded dietary intake and exercise and completed electronic GI symptom and DALDA questionnaires. Large variability in GI symptoms was apparent with no statistical difference in exercise GI symptom frequency or severity and DALDA score. While exercise GI symptoms were not different, daily GI symptoms were lower each day of the low FODMAP dietary period. Short-term FODMAP reduction may be a novel tool in improve daily GI symptoms in healthy runners with exercise-associated GI distress. Future work in this area should incorporate exercise protocols with

higher intensity and longer duration to better assess the impact of this diet on GI symptoms occurring during exercise.

Conclusions

This progressive work has quantified widespread adherence to a GFD amongst NCA. Although, many NCA adhere to a GFD due to beliefs underpinned by unsubstantiated health, GI and performance benefits, a short-term GFD was not found to have a beneficial (or negative) effect on performance, GI health, systemic inflammation or overall wellbeing. FODMAP intake may be consequently reduced with a GFD and is proposed to modulate GI symptoms, rather than gluten itself. Relatedly, elimination of high FODMAP foods were found to be a common dietary strategy employed by athletes aimed at attenuating GI symptoms with high rates of self-reported success. Results from our successive intervention studies showed improvement in GI symptoms with elimination of high FODMAP foods. Based on these findings, FODMAP manipulation, rather than gluten-elimination, may be a more successful and novel intervention to consider for the sport nutrition practitioner's toolbox for management of GI distress in athletes. A practitioner supported systematic and individualized approach will be essential for the potentially successful implementation of these dietary approaches.

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Common Abbreviations

CD	coeliac disease
GFD	gluten-free diet
GCD	gluten-containing diet
IFABP	intestinal fatty acid binding protein
IL	interleukin
LFOD	low FODMAP diet
HFOD	high FODMAP diet
FODMAP	fermentable oligo-, di-, monosaccharides and polyols
NCA	noncoeliac athlete (including athlete without a clinical requirement for a gluten-free diet)
NCGS	noncoeliac gluten/wheat sensitivity

Infrequent abbreviations used throughout the thesis are defined *in situ*.

Chapter 1: Thesis Introduction and Overview

Optimal athletic performance relies on the multifaceted interplay of numerous components including physical training, physiological adaptations, psychological wellbeing and the nutrition strategies to support all of these elements. In athletes, particularly endurance-based, gastrointestinal (GI) distress is a common occurrence (128). Exercise-associated GI symptoms occurring during exercise, and up to several hours afterwards, have the potential to derail training capacity, impair optimal athletic performance as well as subsequent nutritional recovery and performance (37). Dietary modulation and training the gut to tolerate fuels are foremost strategies implemented by athletes with the aim to reduce GI distress (32, 35, 79).

Athletes commonly avoid certain foods or follow dietary regimes with the aim to improve performance and reduce GI symptoms (35, 37). Gluten-free diets (GFD) and elimination of high fermentable oligo-, di-, monosaccharides and polyols (FODMAP) foods have become popular strategies to reduce GI distress (19), however no evidence exists supporting the beneficial outcomes of these dietary practices. GFD are further touted by many to reduce inflammation, improve psychological wellbeing and provide an ergogenic edge (50), again with a lack of scientific evidence in noncoeliac athletes (NCA). Triggers of GI distress involve many factors; however, it is possible that the unique stress placed on the gut from intensive exercise may increase susceptibility to dietary triggers and consequential GI symptoms. Evolving research continues to investigate and integrate novel nutritional approaches to reduce GI distress and thus benefit athletic performance. This thesis follows the following concepts: First exploration and quantification of GFD and high FODMAP food elimination behaviours in NCA. Secondly, human based studies will be the foundation for investigations of the effects of GFDs and FODMAP restriction, primarily on GI symptoms, but also exercise performance

and related parameters, in NCA. Lastly, the seminal findings from the work within the thesis will be tied together with contemporary literature to summarize the current state of knowledge of GFD and FODMAP modification in NCA.

1.1 Background

1.1.1 GI distress in athletes

GI symptoms are reported to occur in 30-50% of endurance athletes and if severe enough, impair training capacity, performance and/or recovery (39, 159). Frequently experienced symptoms include upper and lower GI symptoms, such as: reflux, vomiting, bloating, loose stool, diarrhoea and abdominal cramping (39, 131). Aetiology of GI symptoms is multifactorial involving physiological, mechanical and nutritional elements as well as a likely genetic predisposition (35, 39). During exercise, particularly throughout strenuous bouts, blood flow is shunted to working muscles and blood flow to the gut may be reduced by up to 80% (159). As a result, GI ischemia compromises epithelial barrier function and is recognized as the primary pathophysiology mechanism accountable for the changes in GI permeability and potentiating GI symptoms (167). High-impact mechanics, such as those related to running, can furthermore injure the epithelium alongside postural factors eliciting upper and lower GI symptoms (37, 172). Nutrition intake, the primary focus of this thesis, is also a confounding factor with a significant effect on GI wellbeing (36, 37).

1.1.2 Current nutrition strategies employed to reduce GI symptoms in athletes

Nutritional strategies are often employed as a first-line approach to reduce GI symptoms (117). General strategies include reduced fibre or low residue diets, increasing carbohydrate and fluid tolerance as well as decreasing fat and protein intakes (37). More recently, going gluten-free has seen a global upsurge and a GFD has become an extremely popular dietary strategy touted to improve GI health in athletes. A strict GFD eliminates all forms of gluten; a storage protein

composite (3) found in wheat (gliadin), rye (secalin) and barley (horedin) are the primary peptides associated with immunologic reactions in CD. It is also present in other food products through the addition of grain-based foodstuffs or via cross-contamination (86). Avoidance of gluten is essential for individuals with clinical conditions requiring a GFD and symptoms are generally improved with this diet (142). In NCA gluten avoidance is believed to improve psychological wellbeing, reduce inflammation, improve body composition for sport and provide an ergogenic performance edge. Healthy athletes or NCA, without a clinical necessity for gluten-avoidance, are a predominant cohort adopting a gluten-free lifestyle based on anecdotal beliefs and perceptions around unsubstantiated health and performance benefits (50, 137).

1.1.3 From Gluten to FODMAPs

Adherence to a GFD has become exceedingly prevalent amongst athletes with the aim to reduce inflammation, overall wellbeing and improve GI health (19). Eating a GFD not only eliminates gluten-containing foods but also subsequently decreases consumption of FODMAPs (52, 118). FODMAPs are a family of short-chain carbohydrates that are incompletely absorbed in the GI tract and are rapidly fermented by gut bacteria causing adverse GI symptoms in sensitive individuals, mainly with clinical conditions such as irritable bowel syndrome (IBS) (54). Fructans, in particular, are concentrated in wheat-based foods and are made of fructose molecule chains which are poorly absorbed because the small intestine lacks hydrolases to break their fructose-fructose bond (14, 146). Researchers suggest that FODMAP reduction consequent to elimination of gluten-containing foods may actually be the reason for improved GI symptoms (52, 118). In athletes reporting symptom improvement with the change to a GFD, it may actuallybe the associated general reduction in FODMAP intake tempering GI symptoms. In addition, many athletes, who may or may not eliminate gluten are avoiding foods high in FODMAPs such as lactose or legumes, to reduce GI symptoms (41).

1.1.4. FODMAP reduction as a strategy to reduce exercise-associated GI distress

A low FODMAP diet, which reduces short chain carbohydrate intake, has been implemented with notable success for the treatment of IBS (34, 54, 148). There are several unidentified mechanistic elements potentiating GI symptoms and sensitivity to FODMAPs. However, the symptomology displayed in exercise-associated GI symptoms and IBS is analogous (39, 63). A low FODMAP diet may be appropriate beyond treatment for IBS symptoms and could be a novel tool to reduce GI distress in an athletic context. Ingestion of carbohydrates, particularly solutions with a high osmolality, have been linked to the development of GI symptoms during exercise (131, 136, 159). Short chain carbohydrates' osmotic actions and the presence of pre-existing high dietary FODMAP concentrations in the GI tract may further increase luminal fluid volume, distention and related symptoms experienced by some athletes. Lower in the GI tract fermentation of FODMAPs potentially amplify flatulence, bloating, abdominal pain and diarrhoea, predominantly associated with mechanical jostling and ischemia (55, 148). Although, healthy non-athletic populations have not been shown to benefit from FODMAP restriction, the repeated stress placed on the endurance athlete's gut could increase susceptibility to dietary triggers. Unique training regimes undertaken by endurance athletes' typically include 25 to 30 hours per week of training and even up to 30 to 35 hours per week of competition in events such as the Tour de France (2, 141). This intensive exercise is coupled with ingestion 250 to 300 kcals of energy per hour, primarily consisting of carbohydrate (144) can place extreme stress on the GI system. Intensive exercise stress combined with concentrated carbohydrate intake creates the perfect storm for GI issues in endurance athletes.

1.2.5. Clinical conditions requiring a gluten-free diet

In clinical conditions, such as coeliac disease (CD), wheat allergy and noncoeliac gluten/wheat sensitivity (NCGS) gluten avoidance is necessary to prevent adverse health consequences resulting from the ingestion of gluten peptides. At present, the gold standard protocol for NCGS

diagnosis is the resolution of symptoms upon gluten exclusion and manifestation of symptoms with systematic food reintroduction protocols (27, 30). Using a gluten-challenge to establish NCGS is cumbersome with confounding elements, such as, belief effects and additional subsequent dietary changes that could actually be the modulator of symptom changes. The lack of diagnostic criteria for NCGS has left many athletes self-diagnosing gluten-related conditions based on symptoms or even no symptoms at all. Recently researchers have identified objective biomarkers of systemic immune activation (Immunglobulin (Ig) G, IgA and IgM antibodies, serum lipopolysaccharide binding protein, CD12) in conjunction with compromised intestinal epithelium (fatty acid binding protein) in patients eating a gluten-containing diet and meeting the criteria for NCGS (164). Continued investigation in this area promises to solidify diagnostic criteria in clinical situations. However, in a healthy athletic population it is important to consider if repeated epithelial injury caused by the physiological stress of intensive training (167) potentially increases susceptibility to dietary triggers, such as FODMAPs as compared to non-athletic populations.

1.1.6. Intestinal Permeability and Inflammation

Beyond perceived performance benefits, enhancing gut health and immune system regulation are fundamental reasons why athletes may avoid certain foods or adopt dietary practises. As the largest immune organ in the body the intestinal barrier is of unique importance to athletes, as strenuous training is recognised to compromise this barrier and optimal immune function (77). Increases in intestinal permeability through rearrangement of tight junction proteins result in intestinal barrier damage and alterations in the movement of endotoxins across the lumen of the GI tract into circulation (177). The immune system recognizes endotoxins, which are components of gram negative bacteria, initiating inflammatory cascades (56). Certain inflammatory processes are considered a necessary component of training adaptation. Disproportionate pro-inflammatory cytokine responses have however been associated with

lower GI symptoms (77). Excessive exercise-associated epithelial barrier injury and resulting inflammatory response could theoretically be amplified by gluten and FODMAPs (35, 37, 167), resulting in exacerbated adverse intra- and extra-intestinal symptoms.

1.1.7. Belief Effect Associated with Dietary Interventions

Extending across clinical and sport continuums the belief in the positive effects of an intervention has been evidenced to improve various outcomes, such as perceived GI symptoms and performance (11, 66, 82). In IBS patients, self-reported improvements in GI symptoms resulted even when an openly labelled placebo pill was administered (82). Sport scientists have also established the performance-enhancing effects of belief in a novel intervention and estimated that performance may be relatedly improved by 1-3%, regardless of the establish efficacy (10, 66). Dietary placebos have not been well tested in athletes, however it is reasonable to propose that the novelty of a GFD or special manipulation of high FODMAP foods may result in a positive (placebo) effect on performance, experienced both objectively and/or subjectively (e.g. reduced pain, exertion or GI symptoms) (10, 66) in the field. Placebo effects are used strategically in sport, however, the complications potentially accompanying unnecessary dietary restriction could be unfavourable to health and performance due to issues of dietary inadequacy and other complications (e.g. orthorexic behaviours). Overall, anecdotal experiences reporting the benefits of a GFD for athletes may be consequential of the belief effect and this should be considered when assessing the outcomes of any dietary intervention.

1.1.8. Conclusion

An increasing number of athletes believe avoidance of gluten and food high in FODMAPs are fundamental for optimal GI wellbeing, health and athletic performance (41). Achievement of desired body composition and enhancement of athletic performance are also strong rationales for food avoidance amongst athletes, regardless of the lack of established efficacy of these

practises (19). To date, there is scarce evidence supporting the beneficial effects of a GFD or FODMAP avoidance for healthy athletes. It is easy to dismiss these trends as a 'bandwagon' effect and to justify the reported beneficial outcomes as a result of belief effect or due to other subsequent dietary changes. However, it is plausible that the unique stress placed on an athlete's GI system increases susceptibility to gluten and/or FODMAPs, particularly in endurance athletes. Gluten-free and low FODMAP diets have been successfully implemented in the treatment of clinical GI conditions (4, 152). Commonalities between the physiological mechanisms and symptomology in clinical and exercise associated GI distress support the investigation of these dietary modifications for the management of exercise-associated GI symptoms (39, 53). The primary purpose of this thesis is to investigate if a GFD or low FODMAP diet influences GI wellbeing or parameters influencing performance in healthy endurance athletes, as is widely perceived.

1.2. Significance of the research

GI distress in, primarily, endurance athletes is abundant (30-50%) and can subsequently impair performance. Despite increasing numbers of athletes adopting a GFD or eliminating high FODMAP foods, there is a lack of evidence-based research supporting the efficacy of these strategies. Unnecessary food restriction may compromise optimal fuelling, nutritional status, beneficial gut bacterial populations and generate psychological strain and early stages of orthorexia nervosa. Examination of the effects of GFDs and/or FODMAP restriction to attenuate GI symptoms and related parameters is of significance primarily to determine the efficiency of these diets in NCA. Secondly, evidence-based research is necessary to provide practitioners and athletes trustworthy information to guide decisions surrounding the appropriateness of these dietary regimes. Findings from this research may begin to reconcile beliefs in the beneficial effects of a GFD or FODMAP reduction and offer novel dietary strategies to reduce GI distress and improve performance in athletes.

1.3 Research Aims

The aims of the research presented in this thesis were to investigate:

1. Various beliefs and reasons supporting the popularity and rapid uptake of GFDs as well as high FODMAP food avoidance amongst NCA via questionnaire based approaches.
2. Quantify GFD adherence rates of GFD and high FODMAP food elimination in NC.
3. Efficacy of GFD on performance, GI health, systemic inflammation and perceptual wellbeing via a randomized, placebo-controlled, crossover blinded intervention study.
4. Efficacy of FODMAP reduction as a strategy to reduce GI symptoms in clinically healthy athletes with exercise-associated GI distress in an initial case study intervention followed by a randomized, placebo-controlled, crossover, blinded trial.

1.4 Thesis organization

This doctoral thesis contains a series of four studies which are aimed at quantifying, understanding and determining the effects of GFDs and high FODMAP foods primarily on GI symptoms, as well as inflammation and perceptual wellbeing, as potential parameters influencing performance, in NCA.

Chapter 1: Contains a general introduction of the themes comprising the thesis and expresses the rationale, aims, study designs, and general layout of the thesis.

Chapter 2: The first study utilized an online questionnaire, which was developed to assess the current state of beliefs and GFD adherence rates of NCAs for subsequent human-based dietary intervention studies (research aim 1). Internationally distributed, this questionnaire collected data pertaining to demographics, dietary practises, prevalence rates, beliefs, experiences, GI-related descriptions and sources of information pertaining to GFDs and high FODMAP foods amongst NCA.

An edited version of this manuscript was published as:

Lis D, Stellingwerff T, Shing CM, Ahuja K DK, Fell W J. Exploring the popularity, experiences, and beliefs surrounding gluten-free diets in noncoeliac athletes. Int J Sport Nutr Exerc Metab 2015; 25:37-45.

Chapter 3: The second study and publication followed up on the findings of study one. This double-blind, placebo controlled, crossover dietary intervention assessed the effects of a GFD on athletic performance by investigating several key parameters influencing performance in NCA: GI symptoms, epithelial injury, perceptual wellbeing, systemic inflammation and, the primary outcome, exercise performance (research aim 3).

Lis D, Stellingwerff T, Kitic CM, Ahuja KD, Fell J. No effects of a short-term gluten-free diet on performance in noncoeliac athletes. Med Sci Sports Exerc. 2015; 47(12):2563-70.

Chapter 4: Presents a summary of additional findings from study one (questionnaire-based study) pertaining to elimination behaviours of high FODMAP foods with the aim to reduce GI symptoms in athletes (research aim 1, 2). This is the third publication arising from this thesis.

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Food avoidance in athletes: FODMAP foods on the list. *Appl Physiol Nutr Metab.* 2016;41(9):1002-4.

Chapter 5: To lay the foundation work for investigations of low FODMAP diets in symptomatic athletes this chapter is an innovative case study intervention conducted with a multisport athlete presenting with no functional gastrointestinal disorders but persistent exercise-associated GI distress (research aim 4). This case study compared a low FODMAP nutrition intervention to a habitually high FODMAP diet to assess the efficiency of short-term FODMAP reduction on GI distress during exercise and outside of exercise. The methodology examined through the case study was applied to study four (Chapter 6).

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms. *Int J Sport Nutr Exerc Metab.* 2016. 26(5): 481-7.

Chapter 6: The final study of this thesis presents a single-blinded crossover dietary intervention aimed at evaluating the effects of a short-term high FODMAP compared to a low FODMAP diet on GI symptoms and perceptual wellbeing in clinical health runners with persistent exercise-associated GI distress (research aim 4).

Chapter 7: This chapter is an invited review of the current literature published in 2016 (98) which explores the themes of this thesis. Research converging GFD and FODMAP avoidance in an athlete population was scarce at the outset of this investigation and the inclusion of our seminal work, purposefully positioned towards the end of this thesis, within the literature review, provides a more extensive overview. This chapter first summarizes clinical conditions requiring gluten-avoidance and occurrence rates of these compared those of NCA. Secondly, athletes' perceptions, rationale and experiences in going gluten-free alongside the evidence pertaining to gluten and its effects on GI health, inflammation, athletic performance and body composition are reviewed. Third, GFD nutrition adequacy, psychosocial implications and belief effects are discussed. Lastly, as a progression from GFDs, FODMAPs are introduced and discussed as a potential modulator for GI symptoms in NCA athletes.

> Lis D M, Fell J W, Ahuja K D, Kitic C M, Stellingwerff T. Commercial hype versus Reality: Our current scientific understanding of gluten and athletic performance. *Curr Sports Med Rep.* 2016;15(4):262-8.

Chapter 8: Translation of sport nutrition research is most impactful if it can be succinctly interpreted for use in the field with athletes. This conclusion section presents preliminary applied sport nutrition recommendations for practitioners based on this thesis work as well as potential limitations, proposed future studies and concluding comments.

Some repetition between chapters is the result of these chapters being written as scientific papers for publication in various peer reviewed journals

Chapter 2: Exploring the popularity, experiences and beliefs surrounding gluten-free diets in non-coeliac athletes

An original version of this chapter has been published in the International Journal of Exercise, Sport Nutrition and Metabolism as an original research investigation and appears in the literature as:

Lis D, Stellingwerff T, Shing CM, Ahuja K, DK, Fell J. Exploring the popularity, experiences, and beliefs surrounding gluten-free diets in noncoeliac athletes. Int J Sport Nutr Exerc Metab. 2015; 25:37-45.

Thompson Reuters journal impact factor: 2.2

SJR journal ranking: Q2, 1.03

Altmetrics score: 82

Table 2.2 has been edited by modifying the caption from the published manuscript to better describe the population-based findings and to improve the description of the result.

The acronym gluten sensitivity (GS) has been changed to non-coeliac gluten sensitivity (NCGS) to reflect more recently established terminology.

2.1 Rationale

In recent years, a rapid surge in the uptake of GFDs amongst athletes has prompted the need for a greater understanding of the GFD movement. It is known that gluten-avoidance is a requirement for clinical conditions. However, the number of NCA adhering to this diet for health and performance motives seems to massively exceed the number estimated to clinically require gluten avoidance. Anecdotal reports suggest that NCA adopt this diet with the perception that a GFD is healthier, improves GI wellbeing, body composition and has an ergogenic performance benefit, regardless of the lack of reliable evidence supporting these perceptions. To gain a more comprehensive understanding of the underpinnings supporting

GFD adherence in NCA we conducted an international questionnaire-based study. This preliminary work was the first to describe the demographics and report GFD adherence rates in NCA. Data collected in this study further quantified the experiences, beliefs, perceptions and sources of information pertaining to this diet in both NCA adhering and not adhering to a GFD.

2.2 Abstract

Purpose: Adherence to a gluten-free diet (GFD) for non-coeliac athletes (NCA) has become increasingly popular despite a paucity of supportive medical or ergogenic evidence. This study aimed to quantify the demographics of NCA and determine associated experiences, perceptions and sources of information related to a GFD. **Methods:** Athletes (n=910, female=528, no gender selected=5) completed a 17-question online survey. **Results:** Forty-one percent of NCA respondents, including 18-world and/or Olympic medallists, follow a GFD 50-100% of the time (GFD>50): only 13% for treatment of reported medical conditions with 57% self-diagnosing their gluten sensitivity. The GFD>50 group characteristics included predominantly endurance sport athletes (69.9%) at the recreationally level (32.3%), between 31-40 years of age (29.1%). Those who follow a GFD>50 reported experiencing, *abdominal/gastrointestinal (GI) symptoms* alone (16.7%) or in conjunction with two (30.7%) or three (35.7%) additional symptoms (e.g. fatigue) believed to be triggered by gluten. Eighty-four percent of GFD>50 indicated symptom improvement with gluten-removal. Symptom-based and non-symptom-based self-diagnosed gluten-sensitivity (56.7%) was the primary reason for adopting a GFD. Leading sources of GFD information were: *online* (28.7%), *trainer/coach* (26.2%) and *other athletes* (17.4%). **Conclusions:** Although 5-10% of the general population is estimated to benefit clinically from a GFD a higher prevalence of GFD adherence was found in NCA (41.2%). Prescription of a GFD amongst many athletes does not result from evidence-based practise suggesting that adoption of a GFD in the majority of cases was not based on medical rationale and may be driven by perception that gluten removal provides health benefits and an ergogenic edge in NCA.

2.3 Introduction

For approximately 1-1.5% of the population with coeliac disease (CD), and 0.1% with wheat allergies, a gluten-free diet (GFD) is a necessity, while a GFD is beneficial for an additional 5-10% of the population with clinically diagnosed non-coeliac gluten sensitivity (NCGS) (61, 102, 142). NCGS is defined as the presence of morphological, functional and immunological disorders that respond to gluten exclusion, without the features that define CD (163). Although these types of sensitivities to gluten are different in origin, they are all treated with a GFD (67).

General public adherence to a GFD has grown rapidly in recent years illustrated by a growth rate of 28% from 2008 to 2012 in gluten-free foods and beverages sales in Canada (124). Adherence to a GFD has also increased in prevalence in non-coeliac athletic (NCA) populations for additional reasons including: clinically or self-diagnosed NCGS, the belief that gluten-free is healthier, and/or the belief that elimination of gluten will decrease inflammation and gastrointestinal (GI) distress (67). Many NCA have adopted a GFD for perceived performance and health improvements. These athletes may believe gluten removal is associated with the same health benefits as a GFD for individuals with CD, wheat allergy or NCGS, although to date there is no evidence-based research to support prescription of a GFD for non-clinical populations. Some of the perceived benefits of a GFD in NCA include decreased GI symptoms and fatigue, better performance and increased motivation to train (22). Burks et al (2013), who surveyed 279 endurance cyclists, indicated a GFD to be the most popular special diet among this group. Although approximately 12% of respondents had coeliac disease, 43% reported following a GFD with 84% of this group commenting that deviations from a GFD created self-perceived symptoms detrimental to training. It is unknown if these reported improvements are a function of undiagnosed CD or NCGS, or attributable to the perception by athletes that a GFD benefits performance (22).

GI dysfunction is a common occurrence (15-30%) among endurance athletes and can be attributed to several mechanisms including exercise-induced gut dysfunction and high carbohydrate intake (130, 131). Athletes may avoid gluten as a result of the perception that gluten removal reduces GI dysfunction. While the effect of gluten removal in NCA is unknown, gluten removal in irritable bowel syndrome patients does not seem be an reliably effective approach for symptom reduction (13). Biesiekierski et al. (16), demonstrated that in a population of irritable bowel syndrome patients who believed gluten removal had improved symptoms, only 8% reported gluten-specific symptoms when fed gluten in a blinded crossover trial. Research available on GFD in non-coeliac individuals is further limited to investigations in non-athlete clinical populations with irritable bowel syndrome, which may not accurately reflect a healthy athletic population (13, 16).

Some of the potential negative issues surrounding adherence to a GFD in non-coeliac athletes may include: the restrictive nature of the diet; the risk of suboptimal nutrient intake; increased difficulties with obtaining optimal food abroad for the travelling athlete; the potential diminution of beneficial gut bacterial populations; and, increased food costs (on average of 242% for specialty items (145, 155). To our knowledge, beyond consumer reports, only one study has quantified a GFD in an athlete population (22). Therefore, the aim of this broad-reaching questionnaire-based study was to determine: (1) the demographics of NCAs athletes following a GFD and degree of adherence; (2) experiences and perceptions of a GFD in regards to health and exercise performance; and, (3) the sources of information and types of prescriptions provided for a gluten-free diet accessed by athletes.

2.4 Methods

2.4.1 Participants

Athletes (from recreational to Olympic medallists) were recruited to complete an online survey.

Recruitment was via email to professional and academic networks (Professionals in Exercise, Nutrition and Sport, Dietitians of Canada Sport Nutrition Network, Sport Dietitians of Australia), social media outlets and sport governing bodies (National Sport Institutes, Provincial, State and National sport governing bodies throughout Canada, the United States of America, Australia, Europe and Asia). Informed consent was obtained through completion of the survey; withdrawal was possible at any point and questions could be passed. Participation was anonymous, self-selected and the exclusion criteria included athletes diagnosed with coeliac disease (defined by a clinical diagnosis of CD) and athletes under 18 years of age. Ethics approval was obtained from the University of Tasmania, Social Science Human Research Ethics Committee (H12933).

2.4.2 GFD Survey and Survey Development

The 17-question survey was made available online through Survey Monkey (www.surveymonkey.com) from January 24th, 2013 to March 2nd, 2013 (38 days). The survey collected data relating to five topics (**Table 2.1**) addressing the popularity of GFD amongst athletes: (1) demographics (age, gender, sport, level of competition); (2) GFD adherence, if any; (3) rate of GI symptoms occurrence and additional symptoms attributed to dietary intake; (4) perceptions pertaining to a GFD and athletic performance ascribed to a GFD; and (5) sources of GFD information and advice. Survey questions allowed one or multiple responses to be selected or text to be entered where appropriate. Athletes were permitted to leave questions unanswered.

The survey was developed and refined following feedback from six registered dietitians working in sport nutrition at the National and Olympic level in North America; this feedback included: expand descriptive details for questions addressing level of competition and provide further clarification on rate of GI distress and dietary triggers (see **Table 2.1** for survey

overview). These other recognized dietary triggers were incorporated intentionally to reduce the potential bias of a leading question pointing athletes to select gluten. Survey categories were initially expanded to allow for the collection of a comprehensive range of detailed responses and were subsequently collapsed for some questions upon analysis to appropriately categorize responses. Survey feedback and piloting ensured that representative information was being queried to minimize biases for or against a GFD by expanding questions and response options to include other known food triggers such as short chain fermentable carbohydrates (14).

Table 2.1 Survey topics covered and information queried

Topics	Question Focus
1. Demographics	Age Gender Sport Level of Competition
2. GFD adherence	Description of GFD adherence.
3. Rate of GI and other symptoms attributed to dietary intake	Rate of GI issues during exercise. Viewpoints about a GFD (e.g. reduced inflammation) Experience of symptoms perceived to be associated with dietary intake (e.g. abdominal bloating) Dietary components perceived to cause symptoms (e.g. dairy) Elimination of perceived dietary trigger and result
4. Perceptions of a GFD	Dietary changes perceived concurrent with a GFD (e.g. increased fruit and vegetable intake) Physiological changes perceived concurrent with a GFD (e.g. less fatigue from training) Perceived effect of GFD on performance
5. Sources of GFD information and advice	Description of basis of GFD and advice provided Source of GFD information

2.4.3 Data Management and Statistical Analysis

Some responses were grouped and response categories combined where appropriate prior to data analysis. Reponses to the sport an athlete identified with were grouped into general sport categories based on activity demands (e.g. endurance, power). GFD viewpoints were amalgamated into categories, which included; *GI distress, health parameters* (immune function, inflammation, nutrient absorption), *exercise parameters* (fatigue, recovery, energy) and *only appropriate for individuals with a clinical requirement* (CD or NCGS) categories. Symptoms questions were merged into *abdominal/gastrointestinal*, *nutritional* (nutrient deficiencies, bone density loss, anaemia), *physiological* (numbness, fatigue) and *skin indicators* (rash). If athletes indicated more than one symptom they were reclassified corresponding to the total number of symptoms. Dietary changes were amalgamated into *more conscientious of diet overall, less processed* (which included less sugary foods), *increased fruit and vegetable intake*, *increased gluten-free whole grains*, *more balanced nutrition intake overall* and *no known dietary changes*. Physiological changes were condensed into *improved exercise performance and health* (which included overall healthier, decreased fatigue daily and training-specific, improved recovery post-exercise, decreased muscle soreness/stiffness, better training adaptations), *better body composition* (for sport-specific performance), *decreased GI distress* and *only for individuals with CD or NCGS* (do not experience any gluten-related symptoms, not informed about GFD). Sources of GFD information were combined into *online* (online forums, online academic journals, own research, coeliac disease or gluten-free websites), *trainer/coach* (trainer, coach, chiropractor and physiotherapist), *naturopath*, *other athletes* and *nutritionist/dietitian*. *Dietitian/nutritionist* were merged into a single group, as the distinction between the two professional titles is not clearly delineated worldwide.

Although the survey design targeted GFD adherence in three sub-categories (adherence to a GFD 50-75%, 75-89% and 90-100% of the time) responses frequencies were analogous among

all three groups to support grouping 50%-100% of GFD adherence into one group for analysis. Athletes were categorized into two distinct groups for GFD adherence: GFD<50 athletes who adhered to a GFD less than 50% of the time and GFD>50 athletes who adhered to a GFD over 50% of the time. Logistic regression (STATA version SE12; Statacorp LP, College Station, TX) was used to compare two sets of data, the GFD<50 and GFD>50 groups, for rates of GI distress and physiological/dietary beliefs between the GFD<50 and GFD>50 groups. Comparison results are presented as odds ratio (OR) and 95% confidence intervals (CI), where appropriate.

2.5 Results

2.5.1 Study Participants and Demographics

Nine hundred and twenty-four athletes completed the survey. Twelve athletes were removed due to not meeting the inclusion criteria. Analysis was conducted on 910 athletes (female=528, male=377, no gender selected=5), between the ages of 18 to over 50 years. The athletes were from a broad-range of sports and competitive levels, including 18 World and Olympic medallists. Total responses for sport categories, competitive level and age categories are presented in **Table 2.2.**

Table 2.2 Demographic characteristics of athletes

	GFD<50 (n=535)	**GFD>50** (n=375)
Age	n (%)	n (%)
18-24 years	169 (31.6%)	95 (25.3%)
25-30 years	127 (23.8%)	98 (26.1%)
31-40 years*	126 (23.6%)	109 (29.1%)
41-50 years	64 (12.0%)	48 (12.8%)
>50 years	29 (5.4%)	20 (5.3%)
Sport category	n (%)	n (%)
Endurance*	335 (62.6%)	262 (69.9%)
Power	40 (7.5%)	26 (6.9%)
Skill	10 (1.9%)	11 (2.9%)
Swim/rowing	38 (7.1%)	19 (5.1%)
Intermittent	77 (14.4%)	28 (7.5%)
Weight classified/ aesthetic	19 (3.6%)	7 (1.9%)
Winter	9 (1.7%)	9 (2.4%)
Fitness	7 (1.3%)	13 (3.5%)
Level of competition	n (%)	n (%)
Recreational*	116 (21.7%)	121 (32.3%)
Recreational competitive	122 (22.8%)	9 (2.4%)
Provincial/state	62 (11.6%)	26 (6.9%)
National	104 (19.4%)	60 (16.0%)
International	57 (10.7%)	33 (8.8%)
World/Olympic qualifier	35 (6.5%)	21 (5.6%)
World/Olympic medallist	29 (5.4%)	18 (4.8%)
Professional	10 (1.9%)	5 (1.3%)

GFD<50: athletes adhering to a GFD less than 50% of the time; GFD>50: athletes adhering to a GFD over 50% of the time; *Endurance athletes at the recreational level between the ages of 31 - 40 years most highly representative group to adhere to a GFD over 50% of the time.

2.5.2 GFD Adherence

Fifty-nine percent of athletes followed a GFD less than 50% of the time (GFD<50). Of the GFD<50 group, 10.7% *purchased gluten-free products once in a while*, 9.3% followed a GFD *sporadically* (a few days per month), 0.7% followed a GFD *1-2 weeks before competition* and 38.8% *did not follow this diet at all*. Of the 41.2% (n=375) of athletes that followed a GFD>50,

50% adhered to a *GFD 90-100% of the time*, 7.5% adhered *75-89% of the time* and 42% adhered *50-74% of the time*. Of the athletes in the GFD>50 group, 69.9% were endurance sport athletes (n=262) at the recreational level (32.3%, n=121), with most between the ages of 31-40 years of age (29.1%, n=109; **Table 2.2**).

2.5.3 Information sources

The most prevalent source of GFD information for the GFD>50 athletes were: *online* (28.7%, n=290), *trainer/coach* (26.2%, n=264), *other athletes* (17.4%, n=176), *registered dietitian/nutritionist* (14.4%, n=171), *naturopath* (7.4%, n=75), *other persons with CD* (5.4%, n=36) and *medical professionals* (0.5%, n=3). Athlete level influenced GFD primary information sources. Recreational competitive athletes accessed information primarily from *trainers/coach* (26.9%, n=71) and World/Olympic medallist accessed GFD information primarily from *other individuals with CD* (34.0%, n=18).

2.5.4 Prescription of GFD

Of the GFD>50 athlete group a GFD was prescribed for the following reasons: *self-diagnosed NCGS based on symptoms or no symptoms* (56.7%, n=211), *clinically diagnosed NCGS through gluten-challenge test* (9.9%, n=37) or *irritable bowel syndrome with symptoms thought to be triggered by gluten* (8.9%, n=33), *recommended by coach, trainer, chiropractor, physiotherapist or Paleo diet* (8.9%, n=33), *naturopath bloodwork* (7.0%, n=26), *family history of CD* (3.2%, n=12), other (4.8%, n=18) and *recommended by nutritionist/registered dietitian* (0.5%, n=2) (**Figure 2.1**).

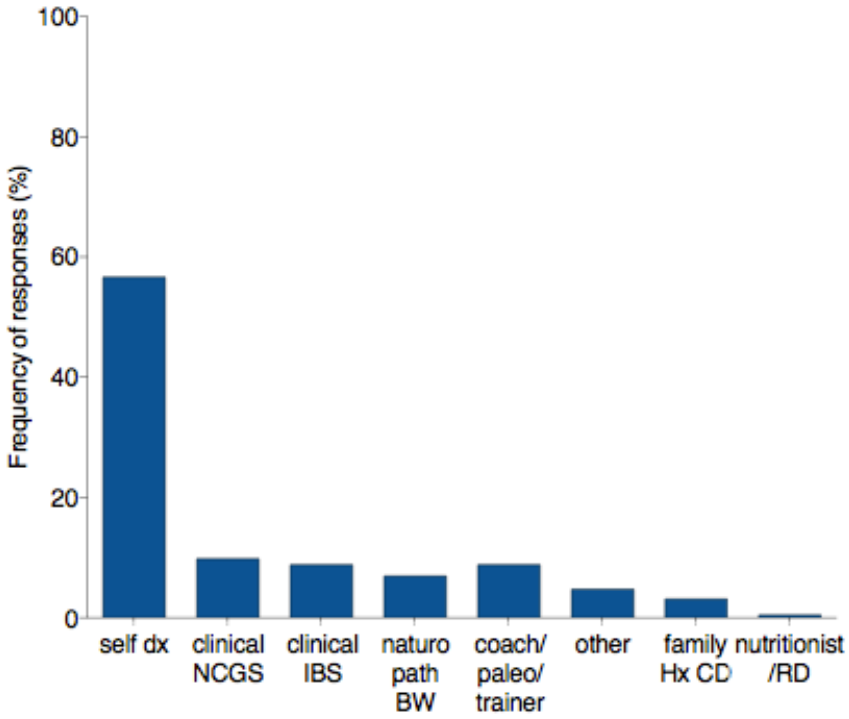

Figure 2.1 – GFD>50 basis of prescription for adherence to a GFD. NCGS: non-coeliac gluten sensitivity, IBS: irritable bowel syndrome, BW: bloodwork, dx: diagnosis, hx: history, CD: coeliac disease, RD: registered dietitian.

2.5.5 Experiences / Symptoms

Gluten removal was reported to resolve physical symptoms including abdominal bloating, gas, diarrhoea and fatigue thought to be triggered by gluten in 80.7% (n=303) of GFD>50 athletes. For 1% gluten removal did not resolve symptoms, and 6.5% had not removed gluten for long enough to determine a change. *Abdominal/gastrointestinal symptoms* alone (16.7%, n=49) and in conjunction with two (30.7%, n=90) or three (35.7%, n=105) additional symptoms were the most highly reported to be triggered by gluten in GFD>50 athletes. Less frequently reported symptoms included *self-prescribed physiological* (2.4%, n=7), *nutritional* (3.3%, n=8), *skin* (0.3%, n=4) and more than 4 symptoms together (10.2%, n=30).

The GI distress occurrence rates were similar (all P>0.12) between the GFD>50 and GFD<50 groups in all categories (**Figure 2.1**). At the GI distress incidence rate of *less than 25%* of the time both groups reported similar frequencies (84.5%, n=452 vs. 80.8%, n=303). Also, comparable between the two groups were reported GI distress rates within the incidence range of *26-50% of the time* (13.6%, n=66 vs. 12.3%, n=51) and *over 50% of the time* (3.2%, n=21 vs. 5.6%, n=17).

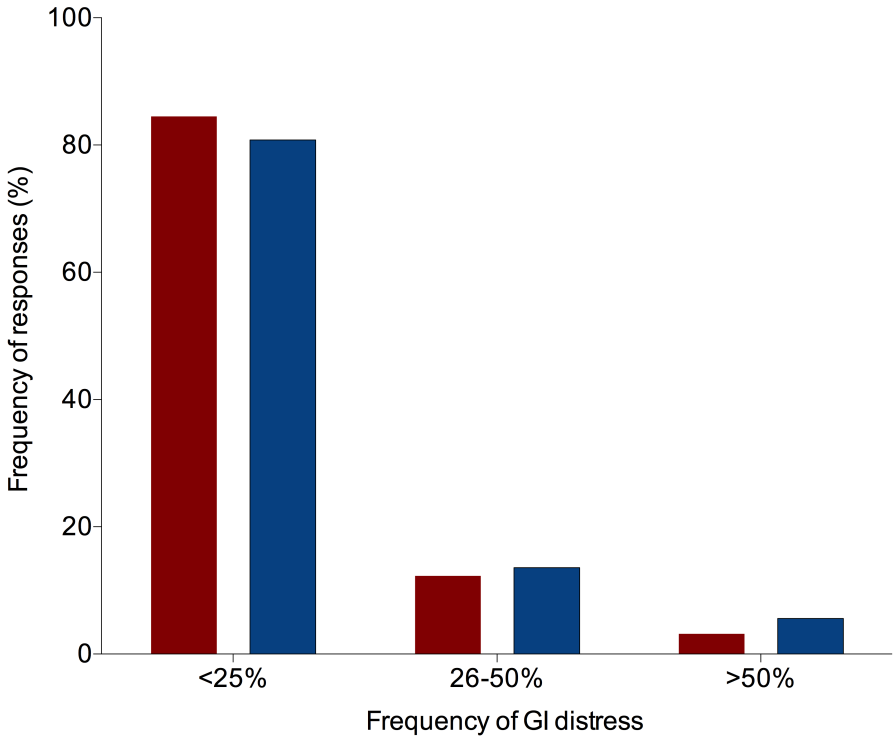

Figure 2.2 – Frequency of gastrointestinal (GI) distress between gluten-free diet adherence gluten-free diet adherence less than 50% of the time (GFD<50 ■) versus 50-100% of the time (GFD>50 ■) groups. Frequency of GI distress are categorized as occurring less than 25% of the time, 26 to 50% of the time and more than 50% of the time.

2.5.6 Beliefs (dietary habits)

The key differences between the GFD>50 and GFD<50 groups in perceived dietary changes that occur alongside a GFD included *more conscientious of overall nutrition intake* (77.9 vs. 58.5%; OR 2.50, 95% CI 1.85 to 3.36, P< 0.001), *less processed food choices* (43.7 vs. 64.5%; OR 0.43, 95% CI 0.32 to 0.57, P<0.001) and *no dietary changes known* (6.9 vs. 8.8%; OR 0.34, 95% CI 0.16 to 0.71, P=0.005) (**Figure 2.3a**). There were no differences between GFD<50 and GFD>50 groups concerning the beliefs that a GFD may also incorporate *increased fruit and vegetable intake* (58.7 vs. 57.8%; OR 1.03, 95% CI 0.70 to 1.35, P=0.78), *increased gluten-free whole grain intake* (41.1% vs. 37.8%; OR 1.14 95% CI 0.87 to 1.5, P=0.31) and *more balanced nutrition intake overall* (33.1 vs. 29.3%; OR 1.19, 95% CI 0.89 to 1.58, P=0.23).

2.5.7 Beliefs (physiological)

Key differences between the GFD>50 and GFD<50 groups were found in perceived physiological changes that occur alongside a GFD. The GFD>50 compared to the GFD<50 group believe more frequently that *improved exercise performance* (56.3 vs. 23.9%; OR 4.09, 95% CI 3.08 to 5.44, P < 0.001); *decreased inflammation/illness* (73.3 vs. 30.3%; OR 6.33, 95% CI 4.72 to 8.50, P < 0.001), *decreased GI distress* (61.1 vs. 30.8%; (OR 3.82, 95% CI 2.87 to 5.10, P < 0.001), *improved body composition for sport performance* (74.4 vs. 43.2%; OR 3.52, 95% CI 2.67 to 4.64, P < 0.001) and *no physiological effects* (2.4 vs. 6.7%; OR 0.34, 95% CI 0.016 to 0.71, P=0.005) occurred alongside a GFD (**Figure 2.3b).** There were no differences between the GFD<50 and GFD>50 groups in the belief that *physiological effects were only applicable to CD or NCGS* (0.3 vs. 1.5%; OR 0.18, 95% CI 0.02 to 1.41, P=0.10).

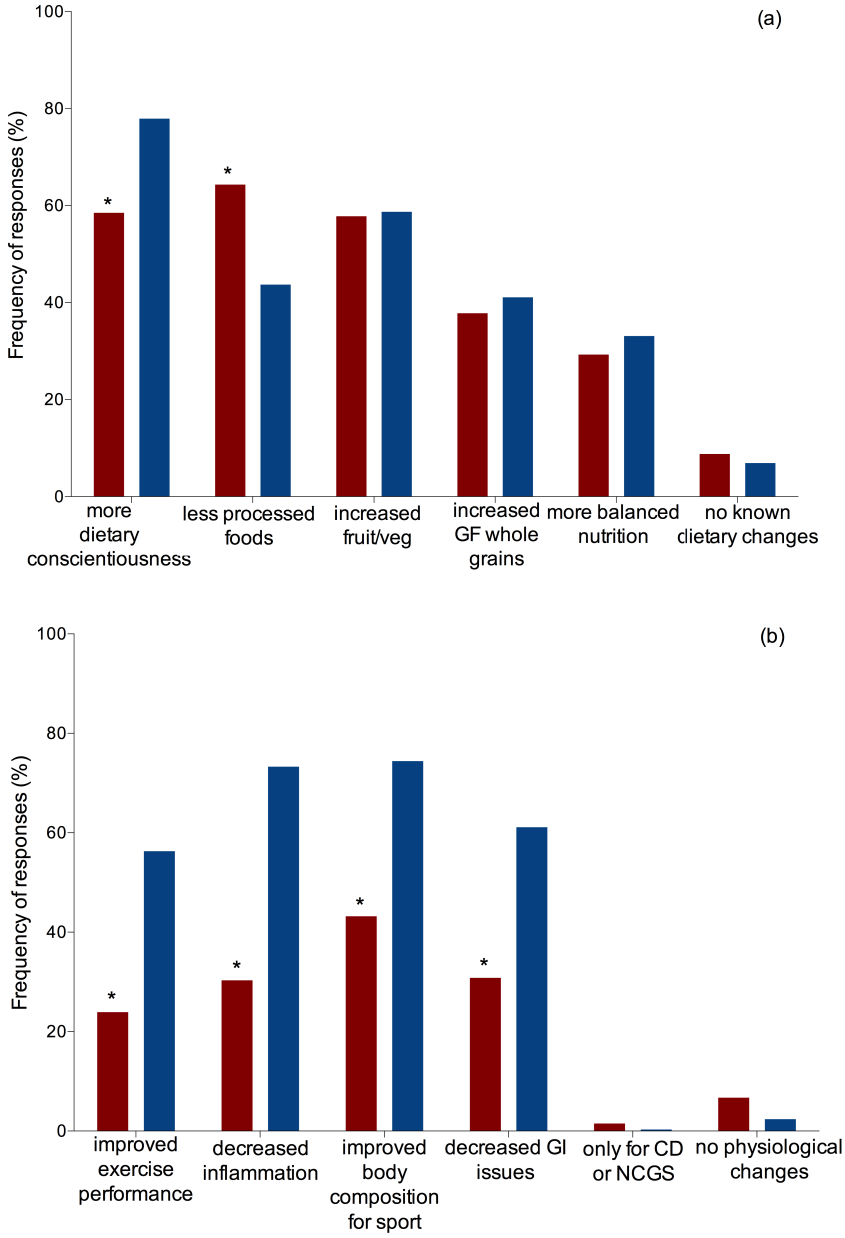

Figure 2.3 – (a) GFD>50 and GFD<50 athletes perceived dietary changes that occur with adherence to a GFD. (b) GFD>50 and GFD<50 perceived physiological changes that occur with adherence to a GFD. *Significantly different between GFD>50 versus GFD<50. CD: coeliac disease, NCGS: gluten sensitivity. *Gluten-free diet adherence 50% – 100% of the time (GFD>50 ■); less than 50% of the time (GFD<50 ■).

2.6 Discussion

Our survey is the first to determine the prevalence of a GFD across a variety of sports and in world-class athletes, which included ~10% world or Olympic qualifiers and/or medallists. Of these we found that 41.2% of athletes adhered to a GFD over 50% of the time and that this diet was most prominent within the endurance sport community amongst athletes at the recreational level (70% of GFD>50) between 31 to 40 years of age. This high frequency of adherence to a GFD over 50% of the time is surprising considering that researchers estimate only 5-10% of the population may benefit medically from a GFD (61). Our survey results further highlight that the decision to adhere to a GFD over half of the time was often not made based on clinical recommendations, but mostly as a result of a self-diagnosed gluten issue (57%). Description of GFD adherence varied from occasionally to all of the time. However, of those who adhered to a GFD over 50% of the time the largest cohort followed this diet 90-100% of the time. Reasons for adhering to a GFD in NCAs include perceived reductions in GI distress, reduced inflammation, improved exercise performance and the belief that the diet supports a favourable body composition for sport.

This survey shows that primarily athletes involved in endurance-based sports adopt a GFD. Burks et al. (22) also found that a GFD diet was the most popular 'special diet' amongst endurance cyclists with similar reports that a GFD was perceived to improved GI symptoms in approximately 80% of survey respondents. The attraction of gluten elimination may be prominent within this sub-group due to the higher frequency of GI dysfunction reported by endurance athletes (15-30%) compared to other types of athletes (78, 130, 131). While exercise may increase intestinal permeability due to reduced splanchnic perfusion, dietary factors such as high carbohydrate intake may also contribute to GI dysfunction (130, 131). There was belief among this athlete-group that gluten removal decreased the rate of GI symptoms (**Figure 2.2b**). Increased rates of GI distress and a greater awareness of nutrition information may also

contribute to the increased popularity of a GFD within this demographic (69, 173).

The GFD>50 athletes reported reductions in abdominal/GI distress to be the primary outcome of gluten-elimination. Abdominal/GI symptoms along with two to three other symptoms, including physiological, nutritional and skin-related symptoms, were perceived to be triggered by gluten and resolved with gluten-avoidance in the majority of GFD>50 respondents. Clinical and case-report data confirms a list of symptoms, such as nutrient deficiencies, abdominal boating and fatigue to resolve with GFD adherence in athletes diagnosed with CD (17). However, alongside CD, a spectrum of gluten-related disorders have been defined. The most well-known of these is NCGS with over 100 associated symptoms, including gluten ataxia, which due to reductions in neurological and muscular coordination would be detrimental to athletic performance (61). According to Gibson & Sheppard (2010) an estimated 15% of the population may have a functional GI disorder, which could be worsened with the intake of dietary triggers. The rise in gluten as a dietary trigger for a range conditions and the upsurge in NCGS and CD may be due to increased awareness and diagnosis of GI and related disorders. However, self-prescription of a GFD based on symptoms or no symptoms was the dominate rationale for gluten-avoidance (~57%) which may or may not be concomitant with gluten itself (52). The rate of GI distress reported in both the GFD<50 and GFD>50 groups was similar and this further demonstrates that the removal of gluten itself may not be the key modulating factor in a GFD and perceived symptom improvements. Given the complexity and importance of an athlete's diet, diagnosis of CD or NCGS should be established before removing gluten from the diet (67). The appropriate diagnoses of NCGS or the medical requirement for a GFD is significant to athletes as this diet can be time-consuming, complex and compromise optimal energy and carbohydrate intake.

In addition to the belief that a GFD reduces GI dysfunction the current study has shown

perceptions among athletes that a GFD improves exercise performance, decreases inflammation, and improves body composition (**Figure 2.3b**). NCA further indicated that other positive dietary factors were believed to simultaneously result from a change to a GFD, such as an increase in conscientiousness of nutrition intake, increased fruit, vegetable and gluten-free whole grains and decreased processed food consumption (**Figure 2.3a**). According to our survey results a small number of athletes believe that decreased energy and carbohydrate intake may result with a GFD which may compromise energy and fuel availability for athletes (101). Given that other dietary factors identified to positively affect heath and performance were believed to happen alongside the adoption of a GFD in NCA it is unknown if reported performance improvements identified were simply perceived, a function of undiagnosed CD, NCGS, other dietary factors, or related to the GFD itself (107, 110, 165). Other dietary changes may occur alongside a GFD and evaluation of any effects of a GFD must take into account other coincidental dietary variations and possible placebo effects (109).

Currently there is a lack of diagnostic criteria for NCGS, where no allergic or autoimmune mechanisms are involved, and NCGS diagnosis is confirmed by gluten-exclusion and followed by monitored reintroduction of gluten-containing foods (142). However, this approach lacks specificity and is subject to the risk of placebo if not blinded (142). The effect size of ergogenic aids and belief in an intervention are similarly estimated to improve performance by 1-3% (66). With the findings that many athletes believe that GFD adherence improves performance for NCAs it is important to consider that belief may influence performance outcomes with this dietary intervention (66). Results from this survey will assist nutrition practitioners to better understand the scope of the GFD movement, to consider the psychological aspects of the NCA athlete following or considering this diet, and the potential placebo affects; all of which are principal nutrition counselling tools to comprehend and apply when working with athletes.

Self-prescription of a GFD among athletes may be reinforced by non-peer reviewed literature or opinions from coaches/trainer of a GFD being overall healthier and improving performance. Non-peer reviewed or anecdotal GFD information was primarily sourced from online resources, other athletes and from coaches/trainers. Nutritionists/registered dietitians were reported much less often as sources of GFD information; a theme common in sport nutrition practise which further highlights that sources of GFD advice may be from non-qualified nutrition professionals (74). Since the avoidance of gluten restricts a range of foods, it has the potential of causing nutrient deficiencies (B vitamins, fibre and iron), compromising gut health by reducing beneficial gut bacteria, especially without appropriate nutrition counselling (49, 145, 147). Further, reduced enjoyment, ease of eating and increased food cost, estimated to be up to 242% higher for a number of gluten-free replacement items, are also an important consideration concerning the appropriateness of a GFD for NCA (70, 155). Although more nutrient dense GF foods are introduced to grocery shelves almost daily, the long-term effects of a strict GFD in NCAs is unknown and it is preferable to assess the necessity of this diet before assigning unnecessary food restrictions.

While our survey excluded individuals with coeliac disease, self-selection may have biased an un-proportional number of responses from athletes interested in or following a GFD. However, the proportionately high rate of athlete respondents that did not follow a GFD, or were unfamiliar with a GFD, support that our findings are most likely representative of an athletic population. Overall, our survey data indicated a high proportion of athletes adhere to a GFD without evidence-based necessity. It is possible that athletes follow a GFD due to perceived physiological improvements that may coincide with other dietary changes and/or the perception that gluten elimination will provide the same health benefits as it does in individuals with a clinical necessity for a GFD. Attractively, perception exists that a GFD provides ergogenic edge in NCA.

An athlete's diet is a key element to training adaptations and athletic performance and all elements affecting nutrition intake must be considered when deciding to adopt a GFD for non-medical reasons. Our survey results indicate that many NCA have adopted a GFD due to perceived, yet unconfirmed, health and performance benefits resultant from gluten removal. Given the restrictive nature of this diet and the unknown effects of long-term adherence to a GFD in NCA, further research in this area is essential to determine the effects of a GFD on parameters of exercise performance and gut health.

Chapter 3: No effects of a short-term gluten-free diet on performance in noncoeliac athletes

This chapter has been published in Medicine & Science in Sport and Exercise as an original research investigation and appears in the literature as:

Lis D, Stellingwerff T, Kitic CM, Ahuja KD, Fell J. No effects of a short-term gluten-free diet on performance in noncoeliac athletes. *Med Sci Sports Exerc.* 2015;47(12):2563-70.

Thompson Reuter journal impact factor: 4.6
SJR journal ranking: Q1
Altmetrics score: 389

3.1 Rationale

This study was conducted to investigate the reported perceptions, beliefs and experiences pertaining to GFD in NCA endurance athletes. Furthering the results from Chapter 2, this double-blind, crossover dietary intervention assessed the effects of a GFD versus GCD on performance and parameters potentially influencing performance, including: GI health, systemic inflammation and perceptual wellbeing. This is the first study to assess the effects of a short-term gluten elimination in NCAs. As a contemporary and topical subject of study, the results from this published manuscript have received international recognition and established a formative presence in the field of sport nutrition as evidenced with an Altmetrics score of 389.

3.2 Abstract

Purpose: Implementation of gluten-free diets (GFD) amongst noncoeliac athletes has rapidly increased in recent years due to perceived ergogenic and health benefits. The aim of this study was to investigate the effects of a GFD on exercise performance, gastrointestinal (GI) symptoms, perceived wellbeing, intestinal injury, and inflammatory responses in noncoeliac athletes. **Methods:** Thirteen competitive endurance cyclists (8 males, 5 females) with no positive clinical screening for coeliac disease or history of irritable bowel syndrome (mean±SD; age: 32±7 years; weight: 71.1±13.4 kg; height 177.0±11.8 cm, VO_{2max} 59.1±8.0 $ml.kg^{-1}min^{-1}$) were allocated to a seven-day gluten-containing diet (GCD) or GFD separated by a 10-day washout in a controlled randomized double-blind, crossover study. Cyclists ate a GFD alongside either gluten-containing or gluten-free food bars (16 g wheat gluten per day) while habitual training and nutrition behaviours were controlled. During each diet, cyclists completed the Daily Analysis of Life Demand for Athletes (DALDA) and GI questionnaires (post-exercise and daily). On day seven cyclists completed a submaximal steady-state (SS) 45-minute ride at 70% peak power followed by a 15-minute time-trial (TT). Blood samples were taken pre-exercise, post SS and post TT to determine intestinal fatty acid binding protein (IFABP) and inflammatory markers (cytokine responses: IL-1β, IL-6, IL-8, IL-10, IL-15, TNF-α). Mixed effect logistic regression was used to analyse data. **Results:** TT performance was not significantly different (P=0.37) between the GCD (245.4±53.4kJ) and GFD (245.0±54.6kJ). GI symptoms during exercise, daily, and DALDA responses were similar for each diet (P>0.11). There were no significant differences in IFABP (P=0.69) or cytokine (P>0.13) responses. **Conclusions:** A short-term GFD had no overall effect on performance, GI symptoms, wellbeing, and a select indicator of intestinal injury or inflammatory markers in noncoeliac endurance athletes.

3.3 Introduction

Gluten-free diets (GFD) are a clinical necessity for 5-10% of the general population for health purposes including coeliac disease, wheat allergy and noncoeliac gluten sensitivity (61). However, general population market reports indicate that the adoption of a GFD has far exceeded the requirement for clinical populations, with GFD uptake exploding amongst noncoeliac athletic populations (58, 97). Correspondingly, our recently published questionnaire-based study, which investigated the frequency, perceptions and beliefs surrounding GFD, found that in 942 noncoeliac athletes over 40% reported following a GFD at least 50% of the time (97). Startlingly, this group of noncoeliac athletes mostly relied on self-diagnosis of a gluten-related disorder and subsequent self-treatment with a GFD (97).

General population gluten avoidance has become prevalent due to a belief that a GFD is "healthier," or owing to self-diagnosed gluten-related gastrointestinal (GI) disorders (42). Noncoeliac athlete populations adopt a GFD in the belief that it is not only healthier and augments weight loss, but will also decrease GI distress and systemic inflammation and improve psychological wellbeing and athletic performance (97). This rise in GFD uptake may be further influenced by advertising campaigns around the medical necessity and health benefits, while athlete testimonies support the idea that at GFD might offer an ergogenic performance edge (103). While there is one study showing improved glucose metabolism and reduced obesity with gluten elimination in noncoeliac rodents (151), there is no scientific evidence to date that shows a GFD positively influences elements of health or performance in non-clinical populations.

Dietary triggers such as wheat (which contains the protein gluten) have been shown to damage the intestinal barrier in clinically sensitive individuals (e.g. coeliac disease (143)). Conversely, high intensity exercise also reduces the integrity of the GI barrier (177). A primary mechanism causing GI distress during exercise is gut ischemia, resulting from the redistribution of blood

from the splanchnic area to tissue with increasing exercise intensities. Splanchnic hypoperfusion ultimately gives rise to a cascade of responsive events including epithelial injury, increased permeability, bacterial translocation and systemic inflammation (87). Recurrent GI stress and injury, which is common among endurance athletes, may create an environment resulting in greater susceptibility to adverse reactions to common dietary triggers (37, 169). GI injury in response to gluten ingestion has been well classified in coeliac disease patients but in noncoeliac gluten-sensitivity this condition is less apparent and evidence varies (45, 120).

Other nutritional changes that may take place subsequent to gluten elimination can either improve or compromise an athlete's diet (97). Athletes believe that GFD adherence increases conscientiousness of eating a healthy and balanced diet (97). However, adopting a GFD without appropriate nutrition counselling may be associated with increased expense, (+242% (49) inadequate intake of B vitamins, fibre and iron, as well as compromised gut health through reduced beneficial gut bacteria populations (49). More recently, Shepherd & Gibson (147) suggest that the inadequacies found in a GFD may be linked to dietary gluten-free food choices rather than the diet itself, which all need to be considered before adopting such a diet.

Given that our published observational data suggests that many noncoeliac athletes have adopted a GFD due to perceived, yet unconfirmed, health and performance benefits (97), our primary aim is to determine the effects of a short-term GFD in noncoeliac athletes on exercise performance. Secondary aims are to determine the effects of a GFD on several parameters that possibly influence performance, including: (1) GI symptoms, (2) perceived wellbeing, (3) intestinal injury, and, (4) systemic inflammation. Our *a priori* hypothesis was that a 7-day GFD would not affect time trial (TT) performance or associated parameters in noncoeliac athletes.

3.4 Methods

3.4.1 Participants

Thirteen competitive cyclists (inclusion criteria: 18-40 years of age, VO_{2max} >60.0 (male) and >50.0 (female) $ml.kg^{-1}min^{-1}$, respectively) participated in this study. A mixed sex cohort was chosen to represent the population adhering to a GFD as presented in our questionnaire-based study (97). Exclusion criteria were: coeliac disease (determined by AGA, tTG IgA, tTG IgG screened by an accredited pathology laboratory); known familial history of coeliac disease; history of wheat allergy; clinically diagnosed noncoeliac gluten sensitivity or irritable bowel syndrome; were following a gluten-free or vegetarian diet, or; had any pre-existing medical condition that could be affected by dietary intervention. Ethics approval was obtained from the Tasmanian Health and Medical Human Research Ethics Committee (H0013244). Prior to inclusion participants were informed about the study procedure, completed a physical activity readiness questionnaire, and provided signed informed consent.

3.4.2 Experimental Design

VO_{2max} Test: Cyclists' maximal oxygen uptake (VO_{2max}) and peak power (W_{max}) were determined using an incremental test to exhaustion on a calibrated cycle ergometer (Excalibur Sport Cycle Ergometer, Groningen, The Netherlands) approximately 10 days prior to the experiment trials. Following a 5-minute warm up at 100W cyclists began an incremental protocol at 100W with increases of 50W for males and 25W for females in 3-minute stages until volitional fatigue. Every 15 seconds of the test expired air was analysed using a metabolic cart (Parvo Medics TrueOne 2400, Salt Lake City, USA) to determine oxygen uptake (VO_2). Heart rate (HR) (RS800CX, Polar Instruments Inc., Oy, Finland), cadence and power output were recorded very 15 second and rating of perceive exertion (6-20 Borg scale) was recorded at the end of each stage (18).

Prior to study commencement a one-time GI history questionnaire and a 24-hour food recall was collected. Utilizing a double-blind, placebo controlled, crossover design participants were randomized by an independent observer according to a computer-generated list to receive either a gluten-containing diet (GCD) or a GFD for seven days, separated by a 10-day washout, and then received the alternative diet. A registered dietitian provided dietary education to participants on label reading, gluten-free eating and nutrition intake recording as participants were permitted to self-select gluten-free foods in addition to the study food provided (i.e. fresh fruits and vegetables, yogurt) stipulating that all food was replicated in the subsequent trial. Exercise performance testing took place on day seven of each dietary intervention and blood samples were taken immediately pre-exercise, post steady state (SS) and post TT.

Gastrointestinal and Wellbeing Monitoring: Throughout the study, three questionnaires were required to be completed each day: (1) post-exercise GI questionnaire, (2) daily GI questionnaire, and (3) Daily Analysis of Life Demands (DALDA). The presence and severity of upper and lower abdominal and other symptoms were determined using a 10-point scale ranging from 0 "no problem at all" to 9 ''the worst it has ever been." Section 1 of the questionnaire addressed upper abdominal symptoms: reflux/heartburn, belching, bloating, stomach cramps/pain, nausea, vomiting. Section 2 addressed lower abdominal symptoms: intestinal/lower abdominal cramps, flatulence, urge to defecate, side ache/stitch, loose stool, diarrhoea and intestinal bleeding. Section 3 addressed other symptoms (dizziness, headache, muscle cramp and urge to urinate) (131). We analysed the frequency of all levels of GI and other symptoms (GI symptoms score 0-9) (131). All standardized GI questionnaires have been utilized in prior exercise and GI symptom research (31, 128, 131).

To assess the general stress levels (Part A) and to determine stress-reaction symptoms (Part B) of the participants the DALDA tool was used (139). This questionnaire requires participants to

rate each variable as "worse than normal," "normal," and "better than normal." Scores were tabulated and the "worse than normal" scores compared between trials. Each questionnaire was completed at the same time of day except for the post-exercise questionnaire, which was completed immediately following training.

Food Preparation: Participants were provided with gluten-free food including lunch and dinner meals prepared and frozen in a gluten-free commercial kitchen (Birdseed Catering), breakfast provisions (gluten-free cereals, breads, muffin, pancake mix), baking staples and snack foods (Orgran, Brookfarm, Byron Bay, PureBred). Participants were permitted to add gluten-free foods to their meals and self-select gluten-free snacks provided dietary intake was replicated for the subsequent trial. The prototype study menu presented a macronutrient profile based on $g.kg^{-1}$ body weight containing carbohydrate 6-8 $g.kg^{-1}$, protein 1.2-1.7 $g.kg^{-1}$ and fat 0.8-1.0 $g.kg^{-1}$ (FoodWorks Professional 7, Xyris, Brisbane, Australia; (138). Two quinoa-based food bars were consumed per day that contained either vital wheat gluten or whey protein. The bars were designed to deliver 16 g of wheat gluten per day (Manildra Group, Gladesville, Australia) or the equivalent dose of whey protein isolate (Vital Strength, Marrickville, Australia). Wheat gluten and whey protein were weighed using a digital food scale accurate to one decimal place (Terraillon, Croissy-Sur-Seine, France). Two food bars containing 8 g gluten each were ingested and spread throughout the day to simulate typical gluten intake patterns. Pilot blinded analysis in 10 healthy individuals, and two pre-trial participants confirmed that the food bars containing gluten could not be differentiated from the gluten-free food bars.

Familiarization to Performance Test: Before the first dietary intervention a familiarization session was undertaken to accustom participants to the testing protocol (91). Information from the incremental exercise test was used to prescribe the intensity of the SS exercise ride: 45-minute SS at 70% W_{max} (169) (234±56 W) followed by a 15-minute TT; a well-established and

validated TT performance measure (76). For the TT the ergometer was set in linear mode where the linear factor was based on individual participant's 70% W_{max} and preferred cycling cadence during the VO_{2max} test (76). We also purposely chose participants were given 0.5 $ml.kg^{-1}$ distilled water every 10-minutes throughout the SS ride.

Performance Test: Preceding each performance testing session participants were provided with guidelines for gluten-free pre-exercise fuelling. Guidelines for a moderate carbohydrate load 24 hours before the performance test were provided which included the study food, self-selected gluten-free food, and instruction for increasing carbohydrate intake. A selection of gluten-free foods was provided to participants for each seven day trial. In combination with this, participants were provided with guidelines for food and fluid intake prior to their performance test. These guidelines included a moderate ingestion of carbohydrate (1-4 $g.kg^{-1}$ body mass) 1-4 hours prior to exercise and 5-7 $ml.kg^{-1}$ body mass fluid in the two hour period before exercise. Participants were permitted to self-select pre-exercise fuels (either provided study meal or snack foods) based on preference and this was evaluated pre-exercise and replicated for each testing session. Each testing session was performed at the same time of day and climatic conditions (20°C, 40% humidity, 767-769 mmHg). Participants refrained from the use of non-steroid anti-inflammatories, caffeine, alcohol and strenuous exercise 24 hours prior to testing.

Prior to the 45-minute SS ride cyclists completed a 5-minute warm-up at 100W. The 45-minute SS ride and 15-minute TT were performed in the same manner as the familiarization and participants were encouraged to complete as many kJ in the TT as possible. During the SS ride verbal feedback on time completed was provided every 5-minutes. During the 15-minute TT, verbal feedback on time completed was given at minute 3, 6 and 9 then every minute for the final 5-minutes, with no other information given. Standardized verbal feedback was provided

with any feedback outside of the script recorded and replicated for the subsequent trial. All verbal feedback and encouragement were provided by the same investigator, standardized and replicated in each trial. Data was collected every 3-minutes for kJ completed, power, cadence and HR.

3.4.3 Biochemical Measurements

At each exercise performance test venous blood samples (5 mL lithium heparin and 5 mL EDTA) were collected from a forearm vein pre-exercise, post SS and post TT. Full blood cell counts were obtained immediately via an automated cell analyser (XS-1000i, Sysmex, Kobe, Japan) while haemoglobin and haematocrit were immediately determined in duplicate using a HemoCue® Hb 20 (HemoCue®, Angelholm, Switzerland) and the capillary centrifugation at 12,000*g* for 5-minutes, respectively. Blood samples were centrifuged at 1000*g* for 15-minutes and plasma was aliquoted and stored at −80°C until analysis. All plasma variables were adjusted for changes in plasma volume (44).

Intestinal Fatty Acid Binding Protein (IFABP): Plasma IFABP, a sensitive and acute marker of small intestinal cell damage, was determined using an ELISA (Hycult Biotechnology, Uden, The Netherlands) according to manufacturer's instructions. All samples were analysed in duplicate with a 5% intra-assay CV.

Markers of Inflammatory Response: Plasma cytokines concentrations of Il-1β, Il-6, IL-8, IL-10, IL-15 and TNF-α were determined using a multiplex bead array assay (Millipore, MN, USA). The minimal detectable concentration of IL-1β was 0.8 $pg.ml^{-1}$, IL-6 was 0.9 $pg.ml^{-1}$, IL-8 was 0.4 $pg.ml^{-1}$, IL-10 was 8.6 $pg.ml^{-1}$, IL-15 was 1.2 $pg.ml^{-1}$, and TNF-α was 0.7 $pg.ml^{-1}$. Samples were analysed in duplicate and the intra-assay coefficient of variation was 9% for IL-1β, 9% for IL-6, 5% for IL-8, 10% for IL-10, 8% for IL-15, 8% for TNF-α.

3.4.4 Statistical Analysis

Before analysis, all data were tested for normality using a Kolmogorov-Smirnov test. Where normally distributed, mixed effects linear regression was performed. When assumptions of linear regression (heteroscedasticity, skewness, kurtosis or linearity) were violated, data were analysed using repeated-measures ordered logistic regression and all analysis were performed for intervention and order effect. Poisson regression was used to compare frequency of GI symptom severity between GCD and GFD daily and during exercise. Analysis was performed using Stata 13.0 (Statacorp LP, College Station, TX). A sport specific Microsoft Excel spreadsheet (73) was used to estimate the likelihood that a GFD would be beneficial, negligible or harmful based upon the smallest important change (5.17 kJ) (76).

Two methods for sample size calculation were applied, including magnitude-based inferential statistics for comparing performance (total kJ completed in 15-minute TT) and power-based sample size calculations for post-exercise IFABP and cytokines. Sample size analysis based on performance was determined using Hopkin's statistical spreadsheet, *Estimating Sample Size for Magnitude-Based Inferences* (72). The spreadsheet estimates sample size requirements when the typical error and smallest important change (Cohen's smallest important effect - 0.2 of the between subject SD) are entered for the primary performance measure. The typical error (6.53 kJ) and smallest important change (5.17 kJ) were obtained from previously published 15-minute TT reliability data (76). Sample size calculation using these values indicated the need for 12 participants. For the blood markers of IFABP and one chosen marker of inflammation (TNF-α), sample size was determined using power calculations to detect an intervention difference at a two-sided 5% significance level with a power of 80%. Assuming a post-exercise IFABP value of 474±74 pg.ml^{-1} (168), and detecting a 20% difference: a total of 10 participants were required. Assuming a post-exercise TNF-α value of 28±4 pg.ml^{-1} (23), and detecting a

10% difference a total of 11 participants were required. Thirteen participants were recruited to allow for one drop out.

3.5 Results

3.5.1 Participants

Thirteen participants (8 males: VO_{2max} 63.7±6.5 $ml.kg^{-1}min^{-1}$, 5 females: VO_{2max} 51.6±2.8 $ml.kg^{-1}min^{-1}$; 32±7 years of age, weight 71.1±13.4 kg, height 177±11.8 cm) completed the study. Blood results were available for 10 to 12 participants. There were no significant differences between males or females for any of the variables measured (P>0.05).

3.5.2 Performance Test

Exercise performance data is shown in **Figure 3.1**. There was no significant difference in total work completed over the 15-minute TT on day-7 between the GCD and GFD (245.4±53.4 kJ vs 245.0±54.6 kJ, P=0.37). Power (267±60 vs 267±57 W, P=0.80), HR (168±9 vs 167±8 bpm, P=0.56) and cadence (94±8 vs 95±8 rpm, P=0.31) were also similar during the TT for both the GCD and GFD trials. Analysis of the performance data (work completed) using magnitude-based inference indicated a 100% "negligible" effect of a GFD on performance.

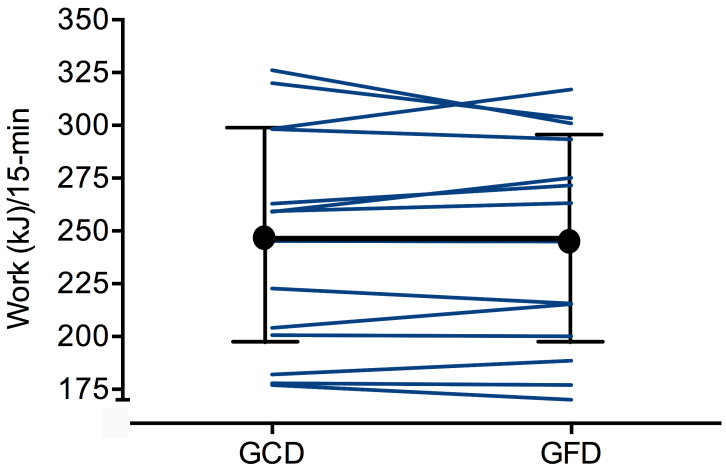

Figure 3.1 – Overall 15-minute time trial performance (kJ) in response to gluten-containing diet (GCD) and gluten-free diet (GFD). — individual performance ● means (SD), n=13.

3.5.3 Gastrointestinal Wellbeing

Frequency of all GI symptoms ratings daily (outside of exercise) and during exercise for upper and lower GI symptoms are displayed in **Figure 3.2**. There were no significant differences in GI symptoms between GCD and GFD for daily upper (P>0.32), lower (P>0.15) and other (P>0.40) symptoms. Similarly, during exercise GI symptoms were not significantly different between dietary interventions for upper (P>0.27), lower (P>0.11) and other (P>0.08) symptoms.

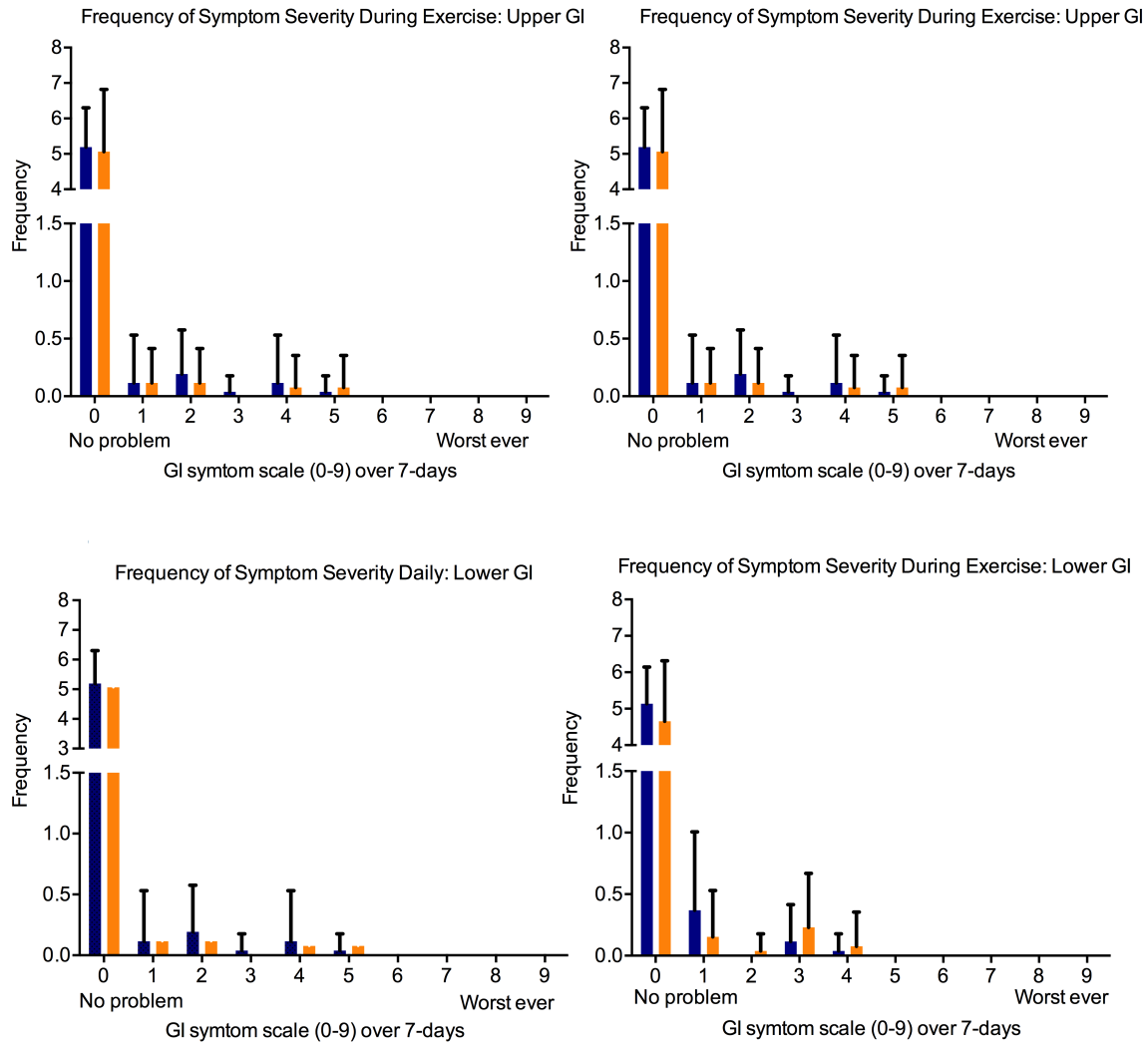

Figure 3.2 – Frequency of GI symptoms daily over 7-day period for gluten-containing diet (■GCD) and gluten-free diet (■GFD). Values are median (range), n=13.

3.5.4 Overall Wellbeing

DALDA scores were tabulated and the "worse than normal" scores were compared between each trial. No difference in the sum of 7-day DALDA scores between the GCD (26±19) and GFD (27±18) was found (P=0.26).

3.5.5 IFABP

IFABP levels increased post SS cycling and post TT from pre-exercise for both groups (GCD and GFD, pre-exercise: 94±83 and 99 ±57 $pg.ml^{-1}$, post SS: 233±188 and 192 ±159 $pg.ml^{-1}$; post TT: 304 ±191 and 301±252 $pg.ml^{-1}$). There were no significant differences in IFABP concentration at any time point between the GCD and GFD (P>0.69).

3.5.6 Cytokines

Plasma concentrations of Il-1β, Il-6, IL-8, IL-10, Il-15 and TNF-α, measured to determine systemic inflammatory responses, were not significantly (P>0.05) different between the GCD and GFD **(Table 3.1)**.

Table 3.1 Cytokines responses from pre-exercise, post steady state (~70% Wmax) and immediately after 15-minute TT after 7-days of a gluten-containing diet versus a gluten-free diet.

Cytokines ($pg.ml^{-1}$)	Diet	Pre-exercise	Post-SS	Post-TT
IL-1β	GCD	7.64 ± 7.73	7.04 ± 6.76	8.17 ± 7.76
	GFD	9.71 ± 9.90	8.64 ± 8.72	9.04 ± 7.69
IL-6	GCD	4.33 ± 4.47	4.42 ± 4.11	6.39 ± 5.33
	GFD	7.21 ± 7.30	6.12 ± 5.73	7.93 ± 4.48
IL-8	GCD	8.83 ± 5.64	11.44 ± 11.34	8.00 ± 4.61
	GFD	10.11 ± 6.74	8.54 ± 3.88	8.75 ± 3.70
IL-10	GCD	14.71 ± 29.74	15.39 ± 24.80	18.53 ± 18.53
	GFD	24.68 ± 37.50	19.48 ± 34.37	18.50 ± 28.76
IL-15	GCD	12.65 ± 9.98	11.49 ± 9.22	12.04 ± 9.74
	GFD	15.17 ± 11.94	14.78 ± 13.94	12.56 ± 8.93
TNFα	GCD	7.77 ± 2.59	7.47 ± 1.77	8.61 ± 1.74
	GFD	10.30 ± 4.88	9.21 ± 3.01	9.26 ± 2.78

Values and mean±SD. There were no statistically significant differences between the gluten-containing diet (GCD) vs gluten-free diet (GFD) pre-exercise, post steady-state (SS) and post time-trial (TT) (n=10).

3.6 Discussion

This is the first study to examine the effects of dietary gluten removal on exercise performance and associated parameters in noncoeliac athletes. Our previous observational data indicated that a much higher proportion of noncoeliac athletes (>40% of endurance athletes, more females than males) follow a GFD than would be required for medical reasons (5-10% of the general population) (61, 97). Belief in a GFD being healthier and reducing GI symptoms and inflammation alongside self-diagnosed gluten-related conditions are the primary motivations for adopting this diet in athlete populations (97). In line with our *a priori* hypothesis, our

double-blind, placebo-controlled, crossover study found no effect of a 7-day GFD on exercise performance. We also found no difference in GI symptoms, overall wellbeing, markers of GI injury or systemic inflammation.

A recent review by Halson and Martin summarized the "belief effect" which suggests the belief in an intervention can contribute a 1 to 3% improvement in performance regardless if it actually has ergogenic mechanisms (66). We have recently shown a current belief in the performance enhancing effects of gluten removal (97). Until findings of the present study, there have been no investigations that have determined the effect of a GFD on exercise performance. Through effective double-blinding, noncoeliac athletes and researchers were unable to differentiate each diet and TT performance was similar between trials (**Figure 3.1**). Accordingly, other physiological parameters such as heart rate, power and cadence were not significantly different between diets. Given a mixed-sex cohort, the potential effects of menstrual cycle on performance were considered, and performance testing for female athletes was scheduled to avoid conflicting with early follicular or the mid-luteal phase. It is further pertinent to note that in undiagnosed coeliac disease or gluten-related clinical conditions, dietary gluten removal would potentially yield a performance benefit through exhibited improvement in biochemical measures and GI symptoms; however, to our knowledge, no published data yet exists to support this.

Performance and training capacity can be affected by GI distress and a decrease in performance has also been shown as a consequence of this stress (121). No difference in GI symptoms was found during the performance test. Across each dietary trial, both exercise associated and daily GI symptoms were also similar (**Figure 3.2**). It has been reported that up to 70% of endurance athletes commonly experience GI distress during intense exercise and that many athletes believe gluten removal might reduce these symptoms (131). Anecdotally, a short-term GFD is

adopted before competition amongst some endurance athletes and many athletes follow a this diet intermittently (97). Short-term clinical interventions in patients with reported GI distress have found that in true noncoeliac gluten sensitivity symptoms triggered by gluten appear within a few hours to days after ingestion (13, 26, 43). Our findings do not support that gluten removal reduces the frequency or severity of GI symptoms daily, while training or during a simulated competitive TT. GI symptom severity in the present study was lower than previously reported during endurance competition (131). Whether a difference in GI symptoms possibly related to gluten would manifest with a more jarring exercise modality, such as running (131), or in environments that further exacerbate GI stress such as prolonged endurance exercise in the heat with fluid restriction, is unknown (88, 89).

Psychological wellbeing is an additional factor that can be influenced by dietary intake and further effect performance and training capacity. We used the DALDA tool to monitor the effects that this dietary intervention had on life stress and stress-reaction associated with athletic performance, and no significant difference in DALDA response was found over a one-week period (139). Although our study is the first to investigate the effects of a GFD on DALDA responses, previous literature has found alterations in psychological wellbeing with short-term dietary interventions (83). Observational data obtained from cyclists on a range of special diets by Burks et al. (22) summarized that 50% of respondents following a GFD reported increased feelings of tiredness/lethargy when deviating from this diet. A nine day dietary intervention of low carbohydrate during a period of intensified cycling has also been shown to increase mood disturbances compared to a high carbohydrate diet (83). The DALDA is as a sensitive tool to monitor wellbeing over a short-term dietary intervention (83) and given that nutritional intake for each trial in the present study was replicated, gluten does not appear to affect wellbeing in noncoeliac athletes.

Gibson & Muir (52) have suggested that gluten itself may not be the sole nutrient regulating factor in the reported symptom improvement with a GFD, but that the subsequent reduction in fructans and galactooligosaccharides (part of the fermentable oligo-, di- and monosaccharides and polyols (FODMAPs) family) associated with gluten removal may be a modulating factor (52). Our study population was dissimilar to the clinical populations observed in the above research and we aimed to design a study with a high degree of ecological validity. Hence, dietary FODMAPs were included in the background diets of the participants, due to the fact that the vast majority of athletes do not comprehensively eliminate all sources of these short chain carbohydrates when following a GFD. Our study design also selected a short-term intervention to minimize the interference with training regime and alongside the evidence that gluten-related symptoms appear, as previously mentioned, in a matter of hours to days in clinical assessment of noncoeliac gluten sensitivity (47). Noncoeliac athletes GFD habits are shown to vary, however a large cohort (42%) only eat gluten-free 50-75% of the time and sometimes only 1-2 weeks before competition (97). Our data indicates that the pattern of short-term or periodic gluten avoidance common for athletes to adopt does not influence performance, GI symptoms or wellbeing (97).

Endurance athletes predictably experience GI ischemia, which is proposed as a primary mechanism causing GI distress during exercise. GI ischemia can ultimately give rise to a cascade of responsive events including epithelial injury and both GI and systemic inflammation (59). In the current study, a submaximal exercise pre-load known to induce GI hypoperfusion was used prior to a 15-minute TT to potentiate a high degree of GI stress (169). Increased epithelial injury also permits translocation of endotoxins across the gut barrier and into circulation, potentially contributing to increased systemic inflammatory responses (77, 177). Pre-exercise IFABP levels were within expected ranges of healthy controls and increased in accordance with similar exercise studies across both dietary trials during the performance test

(169). Increased IFABP levels are indicative of intestinal injury, known to occur under strenuous and acute exercise conditions. It is suggested that intestinal injury is a possible hindrance to training capacity, performance and recovery through adverse GI symptoms and decreased nutrient absorption (169). Our investigation found gut injury to be increased during strenuous exercise; nonetheless, gluten ingestion did not seem to augment this response before, throughout or at the end of a strenuous exercise bought. It is further noteworthy to postulate if recurrent injury, as would occur in endurance training such as in the present study (average training sessions per week, 13), would facilitate an environment of enhanced susceptibility to dietary triggers or influence markers of systemic inflammation in noncoeliac athletes.

Systemic inflammatory responses measured were also similar between dietary interventions before, during and immediately after the performance test. Our data suggests that short-term gluten elimination in noncoeliac athletes does not influence the cytokine response around this specific exercise bout (**Table 3.1**). Interestingly, aside from inflammatory mechanisms associated with strenuous exercise, Soares et al. (151) found that an 8-week high-fat GFD attenuated inflammation associated with adiposity, reduced visceral fat and improved glucose homeostasis in noncoeliac rodents (151). Systemic inflammatory response patterns in both groups paralleled preceding literature with comparable exercise bouts (126), however it is yet to be determine if inflammation localized to the GI tract would be different in noncoeliac athletes.

Future research with a longer duration of GFD adherence may help account for differential gut flora habituation, which could be influential on GI health, performance and other parameters. However, such outcomes may be difficult to monitor, as during a longer intervention, training adaptations would be likely to occur that may mask any dietary influenced performance

changes. Lengthier interventions are also more intrusive for the athlete, compromise dietary adherence, and challenge the ability to control and replicate training and food intake.

Conclusions: In this tightly controlled study, our data suggests that a 7 day GFD does not have a beneficial or a negative effect on cycling performance, GI health, systemic inflammation or overall wellbeing in noncoeliac athletes. Based on these findings it is recommended that athletes seek evidence-based advice before adopting a GFD for non-clinical reasons to ensure that nutrition intake supports individualised and optimal fuelling for sport performance.

Chapter 4: Food avoidance in athletes: FODMAP foods on the list

An original version of this chapter has been published in Applied Physiology Nutrition and Metabolism as a short communication and appears in the literature as:

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Food avoidance in athletes: FODMAP foods on the list. *Appl Physiol Nutr Metab.* 2016;41(9):1002-4.

Thompson Reuter journal impact factor: 2.2
SJR journal ranking: Q2
Altmetrics score: 13

The abstract was modified slightly from the publication above to better explain the study findings.

4.1 Rationale

Adherence to a GFD is reported to improve GI symptoms. Subsequent to the avoidance of gluten containing foods intake of certain FODMAPs are reduced. A decrease in FODMAP ingestion, specifically fructans, may actually be responsible for reported symptom improvement, and not gluten itself. Athletes already individualize dietary regimes with the aim to reduce both acute and chronic GI symptoms and avoidance of high FODMAP foods is becoming an increasingly popular strategy. My questionnaire-based investigation described in Chapter 2 additionally quantified avoidance of FODMAPs and foods high in FODMAPs. This chapter is the first published manuscript to investigate and quantify athlete practices around high FODMAP food elimination with the aim to reduce GI symptoms.

4.2 Abstract

We surveyed 910 athletes to assess behaviours towards self-selected food/ingredient avoidance to minimize gastrointestinal distress. Fifty-five percent eliminated at least one high FODMAP food/category, with up to 64.3% reporting symptom improvement after elimination. In athletes indicating that high FODMAP foods trigger GI symptoms, lactose (88.1%) was most frequently eliminated, followed by fructose (23.8%), galactooligosaccharides (22.4%), polyols (6.1%) and fructans (5.2%). Athletes avoid predominantly lactose and to a lesser extent other high FODMAP foods to reduce gastrointestinal distress.

4.3 Introduction

Gastrointestinal (GI) distress is reported to occur in 30-50% of endurance athletes and has the potential to compromise training capacity and performance (39). Numerous elements can trigger or intensify GI symptoms during exercise including: mechanical, physiological, and dietary factors (39). Dietary elements including high fibre, fat and protein intakes; as well as concentrated carbohydrate loads, have been reported to elicit GI symptoms in triathletes (136). We have previously shown that 41% of athletes avoid gluten and that 81% of these athletes believe gluten-removal reduces GI symptoms (96). Likewise, emerging anecdotal reports indicate that some athletes implement various low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) dietary strategies to alleviate GI symptoms (41). For certain individuals, FODMAPs are poorly absorbed in the small intestine where they increase luminal fluid content and possibly affect gastric motility (54). Poorly absorbed, they subsequently transit to the colon and are rapidly fermented by colonic bacteria causing GI symptoms, such as, diarrhoea, luminal distension and flatulence (123); issues potentially negatively affecting performance.

The aim of this brief communication is to report athlete behaviours in regards to: (1) the elimination of foods/ingredients that are high in FODMAPs; (2) foods/ingredients high in FODMAPs reported to trigger adverse GI symptoms (diarrhoea, bloating, abdominal pain, flatulence); and (3) perceived improvement in GI symptoms consequent to elimination of foods/ingredients high in FODMAPs alone or with gluten elimination. Descriptive data collected from this questionnaire-based study enabled the quantification of self-reported food elimination, specifically high FODMAP foods, amongst athletes with GI symptoms.

4.4 Materials and Methods

4.4.1 Participants

Athletes (n=910, from recreational to Olympic medallists) were recruited to complete an online questionnaire as part of a larger published study examining the popularity, beliefs and experiences of gluten-free diets in non-coeliac athletes (97). Recruitment was international, via email to professional and academic networks and social media outlets. Informed consent was obtained through completion of the questionnaire; withdrawal was possible at any point and questions could be skipped. Participation was anonymous, self-selected and excluded athletes clinically diagnosed with coeliac disease and under 18 years of age. Ethics approval was obtained from the University of Tasmania, Social Science Human Research Ethics Committee (H12933).

4.4.2 Questionnaire Development

As previously described by Lis et al. (94), the 17-item questionnaire run through the Survey Monkey platform from January 24th to March 2nd, 2013, addressed: (1) demographics; (2) GI symptoms attributed to food categories, focusing on gluten and high FODMAP foods, (lactose, fructose, fructans, galactooligosaccharides (GOS) and polyols); and (3) reported GI symptom reduction with offending food elimination. The primary aim of this questionnaire was to explore the popularity, perceptions and experiences of gluten-free diets in athletes, as described in Lis et al. (2014). A secondary aim was to gather data about athletes' experiences and avoidance rates of other foods or dietary constituents that the athletes believed exacerbated their GI distress/symptoms. The lists of foods/categories provided were primarily high in FODMAPs. We also queried high fibre and fat intake, however, for the purpose of this brief communication we have focused on high FODMAP food categories. To avoid bias, the term FODMAP was not used in the survey itself. GI symptoms were described to include abdominal pain, bloating, cramping, flatulence and/or diarrhoea. For data handling and analysis, responses

pertaining to lactose sources, dairy (milk, cheese, yogurt) and lactose (milk, ice cream, custard, soft cheese) were amalgamated into a single lactose category as athletes may use different terminology to refer to the same food category. Excess fructose (apples, mango, honey) and fructose (applesauce, pears, agave) responses were also amalgamated to represent fructose categorically.

4.4.3 Data Management and Statistical Analysis

From the total survey population, the frequency of athletes indicating elimination of each high FODMAP category queried (lactose, fructose, fructans, GOS, polyols) was quantified. **Figure 4.1** shows the arrangement in which the elimination of high FODMAP food information was organized and quantified. The athletes eliminating high FODMAP foods were successively grouped into: (a) athletes that attributed at least one high FODMAP food(s) to GI symptoms but did not necessarily eliminate the offending food; (b) athletes that then eliminated high FODMAP food(s) due to adverse GI symptoms, and; (c) athletes that reported GI symptom improvement with removal of high FODMAP food(s). Frequency analysis (STATA version SE12; Statacorp LP, College Station, TX) was used to analyze the demographics, quantify high FODMAP food(s) elimination, identify the high FODMAP foods reported as GI symptom triggers and subsequent GI symptom improvement with removal. These analyses were conducted in the same manner on those athletes that avoided gluten alongside high FODMAP food(s); **Figure 4.1**).

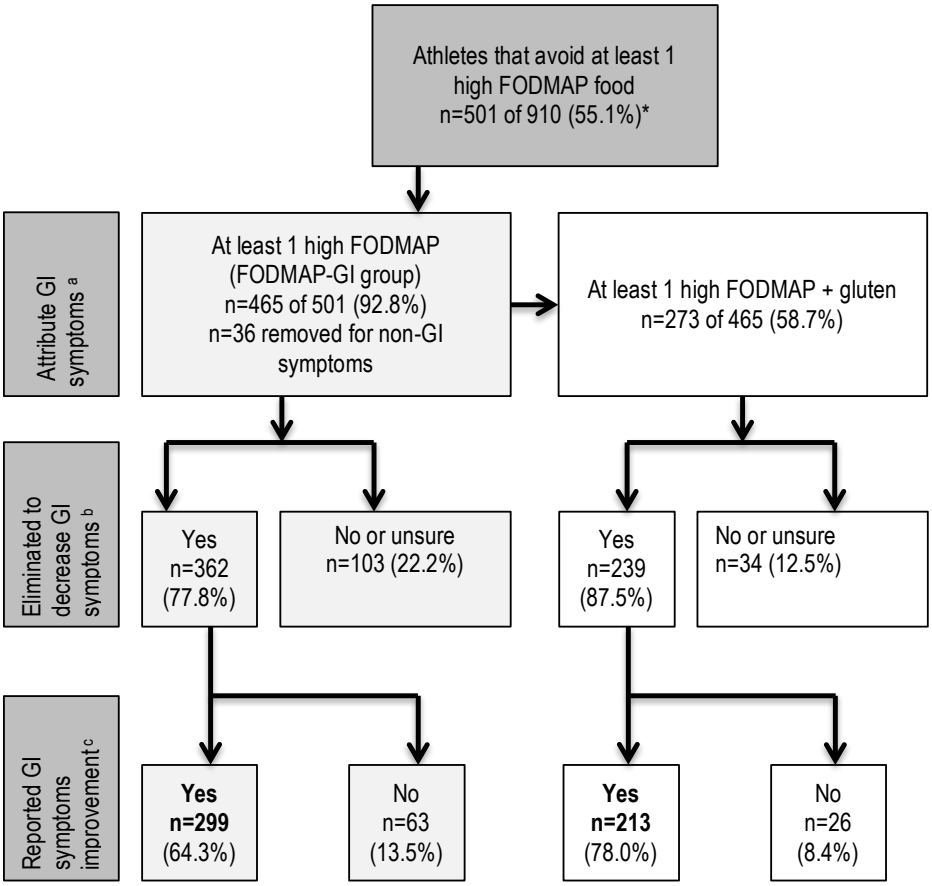

Figure 4.1 – Organization and quantification of FODMAP and gluten analysis.

The left branch shows the frequency individual high FODMAP food or category elimination attributed to GI symptoms and the reported frequency of symptom improvement subsequent to removal. The right branch shows the frequency of individuals that attribute at least one high FODMAP food or category plus gluten to GI symptoms.

*Athletes that avoid at least one high FODMAP food or food category of total questionnaire population.

[a] Athletes that attribute at least one high FODMAP food or food category to GI symptoms.

[b] Athletes that eliminate at least one high FODMAP food or food category due to GI symptoms.

[c] Athletes that report GI symptom improvement subsequent to elimination of at least one high FODMAP food or food category due to GI symptoms.

Unsure=not removed long enough to determine change in GI symptoms.

4.5 Results

4.5.1 Study Participants and Demographics

Demographic information including age, sport-category and competitive level are shown in **Table 4.1**. Nine hundred and twenty-four athletes completed the survey. Fourteen athletes were removed due to not meeting the inclusion criteria (coeliac disease (n=5) or under 18 years of age (n=9). Analysis was conducted on 910 athletes (female=528, male=377, no sex selected=5), between the ages of 18 to over 50 years, from a broad-range of sports and competitive levels, including 47 World and Olympic medallists. Fifty-five percent (n=501) reported avoidance of least one food that can be categorized as high FODMAP. Of this group 64.7% (n=324) were female and 35.1% (n=176) were male (no sex selected, n=1). Of the entire athlete questionnaire population lactose was the high FODMAP food category (44.2%, n=402 of 910) most frequently attributed to lactose-related GI issues. Subsequent elimination of lactose-containing foods was reported by 35.1% (n=319 of 910) of the questionnaire population.

Table 4.1 Demographics of athletes eliminating at least one high FODMAP food

	Athletes eliminating at least 1 high FODMAP food or FODMAP category due to GI symptoms		
	n=465	% of n=465	% of n=910
Sex			
Male	161	34.6%	19.3%
Female	303	65.2.7%	35.6%
Age			
18-24	138	29.7%	15.2%
25-30	123	26.5%	13.5%
31-40	113	24.3%	12.4%
41-50	61	13.1%	6.7%
>50	20	4.3%	2.2%
Sport category			
Endurance	309	66.5%	34.0%
Power	35	7.5%	3.8%
Skill	11	2.4%	1.2%
Swim/rowing	29	6.2%	3.2%
Intermittent	56	12.0%	6.2%
Weight classified/ Aesthetic	7	1.5%	0.8%
Winter	9	1.9%	1.0%
Fitness	9	1.9%	1.0%
Competitive Level			
Recreational	122	26.2%	13.4%
Recreational competitive	111	23.9%	12.2%
Provincial/state	45	9.7%	4.9%
National	84	18.1%	9.2%
International	38	8.2%	4.2%
World/Olympic qualifier	29	6.2%	3.2%
World/Olympic medallist	29	6.2%	3.2%
Professional	7	1.5%	0.8%

Recreational=train but not regularly competitive; recreational competitive=train and race semi-regularly.

4.5.2 GI symptoms attributed to high FODMAP foods and high FODMAP foods plus gluten

Ninety-three percent (92.8%, n=465 of 501) attributed at least one high FODMAP food or category to be linked to negative GI symptoms. The remaining (n=36) indicated that the same foods that are high FODMAP foods triggered other symptoms, such as, skin conditions or

fatigue, which is likely related to other food constituents concurrently present. Of the 92.8% attributing high FODMAP foods to GI symptoms, lactose (86.5%, n=402 of 465) was reported as the largest trigger followed by GOS (23.9%, n=111 of 465), fructose (23.0%, n=107 of 465), fructans (6.2%, n=29 of 465) and polyols (5.4%, n=25 of 465). Gluten alongside high FODMAP food avoidance is shown in **Figure 4.1**. Lactose and gluten together were most frequently attributed to GI symptoms by 52.7% (n=245 of 465) of respondents eliminating at least one FODMAP due to GI symptoms.

4.5.3 Removal of FODMAP the aim to improve GI symptoms

Seventy-eight percent (n=362 of 465) of athletes eliminated at least one high FODMAP food or category from their diet with the intention to improve GI symptoms (**Figure 4.1**). Aimed at reducing GI symptoms lactose was the most highly eliminated (88.1%, n=319 of 362), followed by fructose (23.8%, n=86 of 362), GOS (22.4%, n=81 of 362), polyols (6.1%, n=22 of 362) and fructans (5.2%, n=19 of 362; **Figure 4.2**). Of the athletes eliminating at least one high FODMAP food/category to improve GI symptoms, 82.6% (n=299 of 362) reported symptom improvement (**Figure 4.1**). **Figure 4.1 and Figure 4.2** shows the frequency of reported GI symptom improvement subsequent to high FODMAP food elimination.

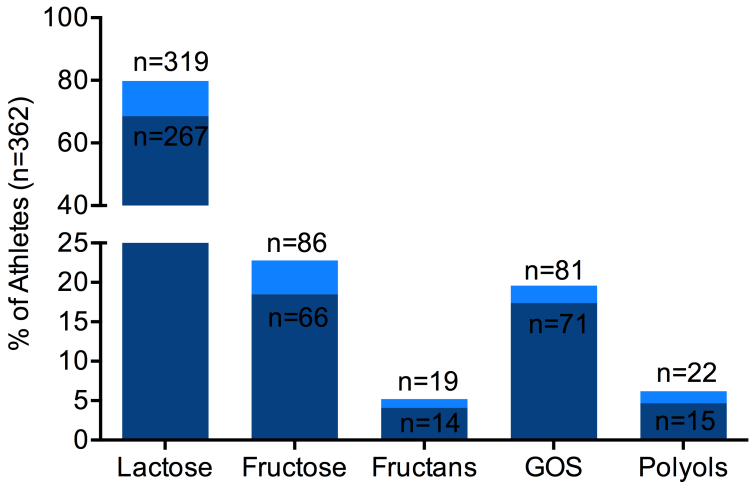

Figure 4.2 – Athletes reporting high FODMAP food category elimination attributed to GI symptoms (■) and subsequent symptom improvement (■); GOS=galactooligosaccharides.

4.6 Discussion

This questionnaire is the first to quantify the number of athletes avoiding foods that are categorized as high FODMAP and to assess the subsequently reported GI symptom improvement. Although our results may be not be more generalizable beyond female endurance athletes due the over representation of this cohort, over half of the questionnaire population reported the elimination of at least one high FODMAP food or category with 93% self-reporting that these triggered adverse GI symptoms. Subsequent to high FODMAP food removal aimed at reducing GI symptoms, athletes reported symptom improvement rates ranging from 68.2% (polyols) to 83.7% (lactose; **Figure 4.2**). The effects of various high FODMAP foods or groups of foods on exercise-induced GI symptoms or in athletes on a daily basis have not yet been investigated. Our study, now confirms that athletes remove sources of lactose, and to a lesser degree other high FODMAP foods, with the intention to improve GI symptoms.

Lactose was the most highly reported FODMAP identified as a trigger for GI symptoms with a correspondingly high frequency of perceived symptom improvements with its elimination (**Figure 4.2**). GI symptoms from lactose-containing foods, can be caused by lactose malabsorption, but can also mask the symptoms caused by other FODMAPs or cow's milk protein allergy (99). Lactose plus gluten elimination were reported by 52.7% of athletes avoiding at least one high FODMAP food or category due to GI symptoms. This finding parallels a recent Australian survey that indicated wheat avoidance to be greatly correlated with dairy avoidance (52.9%) and predicted by sex (female) (176). Gluten avoidance and gluten-free diets have been discussed previously by our research group (96, 97). Our dataset does not allow delineation of the triggering mechanism(s) of undiagnosed functional GI disorders or the possibility of undiagnosed coeliac disease. It is important to acknowledge that the widespread rates of lactose malabsorption are influenced by factors such as ethnicity, genetics, lactase

activity, co-ingested foods, quantity ingested, lactose fermentation pathways and complicating conditions (93, 105, 113). Our observational data identifies that 44.2% (n=402 of 910) of this athlete questionnaire population report lactose-related GI issues and subsequent lactose avoidance (35.1%, n=319 of 910); comparable to the general population (35%) (93). Lactose elimination, as queried in our study, could range from avoidance of all lactose sources or limiting exclusively concentrated sources, or avoidance only prior to training. If athletes are eliminating lactose to reduce GI symptoms, individualized dietary strategies should be applied to ensure adequate calcium intake as this is of concern when eliminating lactose-containing foods (105).

Other high FODMAP foods, including foods or food classifications containing fructose, GOS, fructans and polyols, were reported as GI symptom triggers less frequently. These rates may have been higher with a more comprehensive list of food examples provided within questionnaire (**Appendix 4**). Eliminating fructose containing foods due to GI symptoms was reported in 9.5% (n=86 of 910) of the current study population, which is much lower than the 60% of healthy individuals reported by hydrogen breath test to malabsorb a dose of ≥40 g of fructose (135). The lower rates found in our data may be due to the fact that in habitual eating fructose is often co-ingested with other sugars, which enhances absorption (150). Fructose malabsorption rates calculated using breath testing techniques may report higher frequencies compared to symptom-based estimates as positive breath tests can occur in the absence of GI symptoms (150). However, fructose has garnered particular attention as consumption of high doses or in excess of co-ingested glucose has shown fructose to be incompletely absorbed and cause bloating, abdominal pain/discomfort and flatulence (135). In populations with fructose intolerance, adherence to a reduced fructose diet has decreased GI symptoms (80). Furthermore, athlete populations may consume high fructose intakes as fructose is a common ingredient in sports foods and fruits (e.g. ripe bananas, watermelon, apples), may be consumed

in elevated quantities to meet athlete energy demands, and are popular staples at race feed stations. Nonetheless, our results indicate that athletes report less fructose-containing food elimination to reduce GI symptoms when considering population-based malabsorption rates. For individuals restricting fructose-containing foods, strategies shown to attenuate fructose-induced GI symptoms including eating balanced macronutrients or glucose alongside fructose could be implemented to increase fructose tolerance and minimize dietary restriction (135).

Fructan-containing foods may also be of particular concern for athletes as these carbohydrates are commonly found in wheat products. Only 5% of fructans are digested in all individuals, which may augment GI symptoms during exercise. Our previous research has quantified that 41% of non-coeliac athletes follow a gluten-free diet, and that 81% of these athletes attribute reduced GI symptoms to gluten removal (97), despite our intervention study finding no difference in GI symptoms with a gluten-free diet (96). However, available literature suggests that it is the reduced fructan and GOS quantity in a gluten-free diet that modulates GI symptoms and not gluten-itself (52, 118). It is pertinent to investigate if the generally higher fructan content or other constituents of wheat versus gluten-free grain products (14, 52) augment GI symptoms, as many sport foods are wheat-based and some athlete's diets are heavily reliant on wheat-based foods to meet carbohydrate demands.

Conclusions: This is the first study to investigate dietary habits surrounding the elimination of foods high in FODMAPs to reduce reported GI symptoms in recreational to Olympic and World-class level athletes. With the aim to decrease GI symptoms, over 50% of athletes report avoiding at least one high FODMAP food source or FODMAP category: predominantly lactose (and dairy) and fructose. Athletes' guts are under repetitive stress and may be more susceptible to GI symptom triggers such as short-chain carbohydrates or the high fibre or lactose content inherent in some high FODMAP foods. Unnecessary dietary elimination, without appropriate

food substitutions, should also be carefully evaluated as inadequate nutrient and prebiotic intake may risk optimal fuelling and compromise healthy gut bacterial populations (62). This novel data provides essential underpinning evidence to support the future investigation of individualized approaches to investigate the effects of certain high FODMAP foods, predominantly lactose, in athletes with persistent exercise-induced GI symptoms.

Chapter 5: Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms

An original version of this chapter has been published in the International Journal of Sport Nutrition and Exercise Metabolism as a case study and appears in the literature as:

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Case Study: Utilizing a low FODMAP diet to combat exercise-induced gastrointestinal symptoms. *Int J Sport Nutr Exerc. Metab.* 2016. 26(5): 481-7.

Thompson Reuters journal impact factor: 2.2
SJR journal ranking: Q2
Altmetrics score: unavailable

5.1 Rationale

Elimination of high FODMAP foods with the aim to reduce GI distress is a strategy already employed by half of the athlete population surveyed in the earlier questionnaire-based study (Chapter 4). Conventional sport nutrition recommendations commonly suggest that lactose may be problematic if ingested prior to intensive exercise. Beyond lactose, the potential role of FODMAPs in healthy athletes without IBS, but with exercise-induced GI injury and consequential symptoms is unknown. Frequently athletes implement nutrition strategies before the effects have been assessed scientifically. With this in mind, and the comparable symptomology reported in IBS patients and athletes with exercise-associated GI distress, this single athlete case study investigated the effects of a short-term low FODMAP diet intervention in a multi-sport athlete with persistent exercise-associated GI symptoms. This case study also purposefully established methodology for a crossover low vs high FODMAP dietary trial (Chapter 6).

5.2 Abstract

Purpose: Athletes employ various dietary strategies in attempts to attenuate exercise-induced gastrointestinal (GI) symptoms to ensure optimal performance. This case-study outlines one of these GI-targeted approaches via the implementation of a short-term low FODMAP (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) diet, with the aim to attenuate persistent running specific GI symptoms in a recreationally competitive multisport athlete (male, 86 kg, 57.9 $ml.kg.min^{-1}$ VO_{2max}, 10-15 $hrs.week^{-1}$ training, with no diagnosed GI disorder). M**ethods:** Using a single-blinded approach a habitual diet was compared to a 6-day low FODMAP intervention diet (81 ± 5g vs 7.2 ± 5.7g $FODMAPs.day^{-1}$) for their effect on GI symptoms and perceptual wellbeing. Training was similar during the habitual and dietary intervention periods. Post-exercise (*During*) GI symptom ratings were recorded immediately following training. *Daily* GI symptoms and the Daily Analysis of Life Demands for Athletes (DALDA) were recorded at the end of each day. **Results:** *Daily* and *During* GI symptom scores (scale 0-9) ranged from 0-4 during the habitual dietary period while during the low FODMAP dietary period all scores were 0 (no symptoms at all). DALDA scores for 'worse than normal' ranged from 3-10 vs 0-8 in the habitual and low FODMAP dietary periods, respectively, indicating improvement. **Conclusions:** This intervention was effective for this GI symptom prone athlete; however, randomized-controlled trials are required to assess the suitability of low FODMAP diets for reducing GI distress in other symptomatic athletes.

5.3 Background

Gastrointestinal (GI) symptoms are common in up to 70% of endurance athletes (38), and aside from mechanical, psychological and physiological triggers, several dietary factors are believed to influence symptoms (39). Strategies to improve GI symptoms in athletes include: lower fibre (low residue) or fat intake; reduced fructose load; minimizing dehydration, and; consuming multiple transporter carbohydrates (39). Training the gut to tolerate increased amounts of carbohydrate and fluids has also been shown to increase carbohydrate oxidation and may theoretically reduce the likelihood of GI distress (32). In some cases, regardless of the intervention, GI symptoms persist and novel individualized dietary approaches need to be employed. In the current case study, conventional interventions to reduce exercise-induced GI symptoms were unsuccessful. Therefore, a dietary approach utilizing a low FODMAP (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) diet was trialed over 6-days (3-day lead-in and 3-days of intense running-dominant training) in an attempt to mitigate GI issues.

FODMAPs, a family of short-chain carbohydrates, are in foods including wheat (fructans), pears (excess fructose), cow's milk (lactose), legume beans (Galactooligosaccharides; GOS), and nectarines (polyols) (148). A low FODMAP diet is often implemented in clinical practice as a potentially efficacious treatment for irritable bowel syndrome (IBS; (54, 148). In IBS patients, the malabsorption of FODMAPs increases colonic fluid and gas, which subsequently may trigger or amplify GI symptoms including bloating, flatulence, abdominal pain, loose stool or diarrhoea (152). The GI-related symptomology experienced in individuals with IBS is analogous to those reported by athletes under conditions of exercise stress where splanchnic hypoperfusion, gut ischemia, altered motility, reduced intestinal absorption and mechanical factors compromise gut integrity (55, 167). Despite some GI-adaptions in trained individuals, splanchnic blood flow is still reduced by up to 80% at 70% VO_2max (133). Given the

compromised gut environment common during strenuous exercise (159), it is plausible that high intakes or residual presence of FODMAPs in the colon may trigger or amplify GI symptoms during or after exercise. This case study intervention is an attempt to assess the impact of a low FODMAP diet on a recreationally competitive athlete with persistent exercise-induced GI distress. The outcome was favorable and provides an impetus for larger systematic research of low FODMAP diets in athletes with GI distress.

5.4 Presentation & Assessment of Athlete

This 31-year old recreationally competitive athlete (86 kg, 183.7 cm, 10% body fat, 57.9 ml.kg.min^{-1} VO_{2max}, training 10-15 hrs.week^{-1}) has a history of GI distress and is currently training for multisport events, culminating with Ironman Melbourne 2016. Ongoing nutrition support by an accredited sport dietitian (lead author) revealed persistent GI symptoms during and after high intensity or endurance training (heart rate >155 bpm or training >60-minutes), primarily experienced during running. Previous screening was negative for coeliac disease (tTg IgG and tTg IgA antibodies) and there was no history of self-reported functional bowel disorders, self-diagnosed GI condition or food intolerance. Prior self-implemented interventions aimed at reducing GI symptoms included: avoidance of spicy foods and caffeine before training, and sports drink and all foods during training. He had also previously trialled a gluten-free diet (GFD) without success. It is not possible to quantify the fructan or GOS intake during that GFD period. Consequently, FODMAPs were considered as a potential symptom modulator (118) and investigated.

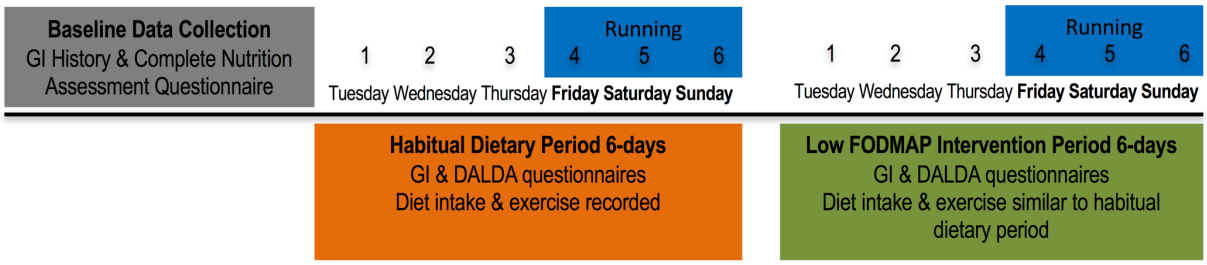

Figure 5.1 – Case study intervention timeline.

After the collection of the screening information, an assessment of FODMAP intake via Complete Nutrition Assessment Questionnaire (CNAQ; Barrett & Gibson, 2010) and background GI symptom questionnaire evaluation, quantifying frequency of symptoms (0 "never" to 9 "always) was conducted (96, 130). The presence and severity of upper and lower abdominal symptoms were determined using a 10-point scale ranging from 0 "no problem at all" to 9 ''the worst it has ever been", as previously applied (96). The response from the background GI symptom questionnaire indicated moderate to severe (>4) upper and lower abdominal symptoms (**Table 5.1**). FODMAP intake was estimated to be 50.8 g FODMAP.day^{-1} (**Table 5.2**), which is considered to be a high FODMAP diet (123). Based on the result of the background GI questionnaire and CNAQ analysis the athlete was requested to record a detailed habitual diet and exercise log alongside questionnaires assessing GI symptoms and perceptual wellbeing.

5.4.1 Habitual Dietary Period

The 6-day habitual diet was analysed for FODMAPs, average energy and macronutrient intake (FoodWorks Professional 7 Xyris, Brisbane, Australia; **Table 2**). During the habitual diet, GI symptom questionnaires were completed at the end of each day (*Daily*; GI symptoms occurring outside of exercise) and also immediately post-exercise (*During*; GI symptom occurring during exercise). Information about life stressors and symptoms of stress were also collected daily using the Daily Analysis of Life Demands in Athletes (DALDA) over a range of training sessions, including cycling, swimming, and various running intensities/durations. DALDA requires participants to rate each variable as "worse than normal," "normal," and "better than normal" and is a pragmatic tool to evaluate stress and stress response (139).

Table 5.1 Baseline, *Daily* and *During* GI symptoms scores for running training days

Section Symptom	Background (Baseline)	Habitual		Low FODMAP	
Daily		Min		Min	Max
Upper					
Reflux/Heartburn	2	1	2	0	0
Belching	2	1	2	0	0
Bloating	4	1	3	0	0
Upper abdominal cramp	4	0	1	0	0
Vomiting	0	0	0	0	0
Nausea	0	0	0	0	0
Lower					
Lower abdominal cramp	4	1	3	0	0
Side stitch	2	0	2	0	0
Flatulence	7	3	4	0	0
Urge to defecate	5	0	3	0	0
Diarrhoea	5	0	0	0	0
Intestinal bleeding	0	0	0	0	0
During Exercise					
Upper					
Reflux/Heartburn		0	2	0	0
Belching		0	2	0	0
Bloating		0	0	0	0
Upper abdominal cramp		0	0	0	0
Vomiting		0	0	0	0
Nausea		0	0	0	0
Lower					
Lower abdominal cramp		0	3	0	0
Side stitch		0	3	0	0
Flatulence		0	4	0	0
Urge to defecate		0	3	0	0
Diarrhoea		0	3	0	0
Intestinal bleeding		0	0	0	0

*Day 4,5 and 6 of the habitual and Low FODMAP dietary periods

GI symptom scores >4 are considered moderate to severe.

5.4.2 Low FODMAP Intervention

To minimize potential bias of reported GI symptoms, the athlete was blinded to the intervention. This was achieved by informing the athlete that 'specific carbohydrates' would be modified in the intervention period but that the intervention may worsen, improve or have no effect on symptoms. This dietary intervention period took place the week following the

habitual dietary period on identical days of the week with similar training loads (Tuesday-Sunday).

Nutritional intervention consisted of a detailed meal plan that replicate the foods, nutrient profile and fluids taken during the habitual period, but exchanged high FODMAP foods for alternative foods low or void of FODMAPs. For example, habitual breakfast consisted of dried fruit and nut muesli with cow's milk yogurt and milk. The intervention low FODMAP breakfast included low FODMAP muesli, consisting of a small quantity of oats, seeds, puffed rice mixed with lactose-free yogurt and milk.

Training was also replicated throughout both dietary phases to ensure the stress placed on the gut was consistent. Training was monitored and closely replicated using Garmin Connect and included: swim 60-minutes (Tuesday); cycle 60-minutes (Wednesday); rest (Thursday); run intervals 70-minutes (Friday); cycle 180-minutes and steady state run 65-minutes (Saturday) and; run intervals 65-minutes (Sunday). Three days of a low FODMAP diet leading into the first of three running-focused training days was chosen with the goal to transit any residual FODMAPs through the gut before the first strenuous running day (Friday). Dietary and exercise log, GI symptoms and DALDA questionnaires were recorded and analysed in the same manner as the habitual dietary period.

Table 5.2 Composition of dietary intake during the habitual and low FODMAP dietary periods

Dietary Component	CNAQ Background macronutrient and FODMAP intake	Habitual	Low FODMAP
Total energy (kcal)	2456	2586 ± 416	2527 ± 407
Total carbohydrate (g)	242	295 ± 68	303 ± 69
Total protein (g)	119	136 ± 9	132 ± 24
Fat (g)	93	88 ± 22	85 ± 28
Fibre (g)	25.9	34 ± 9	33 ± 6
Total FODMAPs (g)	**50.8**	**81.0 ± 5.0**	**7.2 ± 5.7**
Fructose (g)	23.5	20.9 ± 7.9	8.8 ± 4.0
Excess fructose (g)	3.4	0.5 ± 0.6	0.3 ± 0.1
Lactose (g)	42	70.3 ± 3.1	0.5 ± 0.7
Total oligosaccharides (g)	3	7.1 ± 3.9	6.2 ± 6.0
Fructooligosaccarides (g)	1.6	6.5 ± 4.0	5.9 ± 5.7
Galactooligosaccarides (g)	1.2	0.6 ± 0.2	0.3 ± 0.5
Raffinose (g)	0.3	0.4 ± 0.2	0.3 ± 0.5
Stachylose (g)	0.9	0.2 ± 0.1	0.1 ± 0.1
Total Polyols (g)	2.6	3.1 ± 2.2	0.2 ± 0.4
Sorbitol (g)	1	0.3 ± 0.2	0.2 ± 0.3
Mannitol (g)	1.6	2.7 ± 2.1	0.0 ± 0.1

Dietary macronutrients and fibre were calculated using FoodWorks dietary software, which is based on the Australian Food Composition tables. Total FODMAPs = excess fructose + lactose + sorbitol + mannitol + fructans + galactooligosaccharides (GOS). All values are represented as mean (SD) for the two 6-day dietary periods (habitual and low FODMAP intervention). Bold text indicates additive constituents for total FODMAPs.

5.5 Outcomes

5.5.1 Nutrient & FODMAP Intake

Daily food intake was effectively replicated from the habitual dietary record with the only meaningful variance being in FODMAP foods (**Table 5.2**). FODMAP intake during the habitual diet was 81.0 ± 5.0 g FODMAPs.day^{-1} while the intervention diet provided 7.2 ± 5.7g FODMAPs.day^{-1}.

5.5.2 GI symptoms (Background, Daily & During exercise) & DALDA

Table 5.1 shows individual minimum and maximum symptoms scores reported for *Daily* and *During* GI symptoms for days 4, 5 and 6; the days when strenuous running training sessions were completed and GI symptoms were more severe. Compared to the habitual diet, the *Daily* GI symptoms severity scores were lower on the low FODMAP diet (0-4 during vs 0; no symptoms at all); indicating a measureable improvement (**Table 5.1**). Similar improvement was observed for the *During* GI symptom severity scores (0-4 during the habitual diet vs 0; no symptoms at all during the low FODMAP diet). DALDA scores of "worse than normal" ranged from 3-10 (average 6.1) during the habitual diet compared to 0-8 (average 3.7) during the low FODMAP diet. The cumulative GI symptoms scores for *Daily* and *During* (**Figure 5.2**) further show that total symptoms scores were higher each day of the habitual diet than on the low FODAMP diet. This illustrates higher *Daily* and *During* GI symptoms throughout the habitual diet on intensified running days. However, on day 6, *During GI* symptoms scores were zero for the habitual diet. This may have been the result of the self-selected breakfast (eggs, milk, banana) on the day-6 (pre-exercise meal) being lower in fructan and lactose content compared to his usual breakfast (muesli, milk and yogurt). It is plausible that the lowered FODMAP quantity in breakfast on day-6 contributed to the absence of *During* GI symptoms in the habitual period. Although during the habitual dietary period GI symptoms scores were predominantly minor, the athlete, blinded to the intervention, verbally confirmed an improvement in symptoms supported by his statement; "symptoms were remarkably better compared to habitual period and were basically non-existent during exercise or during the day throughout the intervention period."

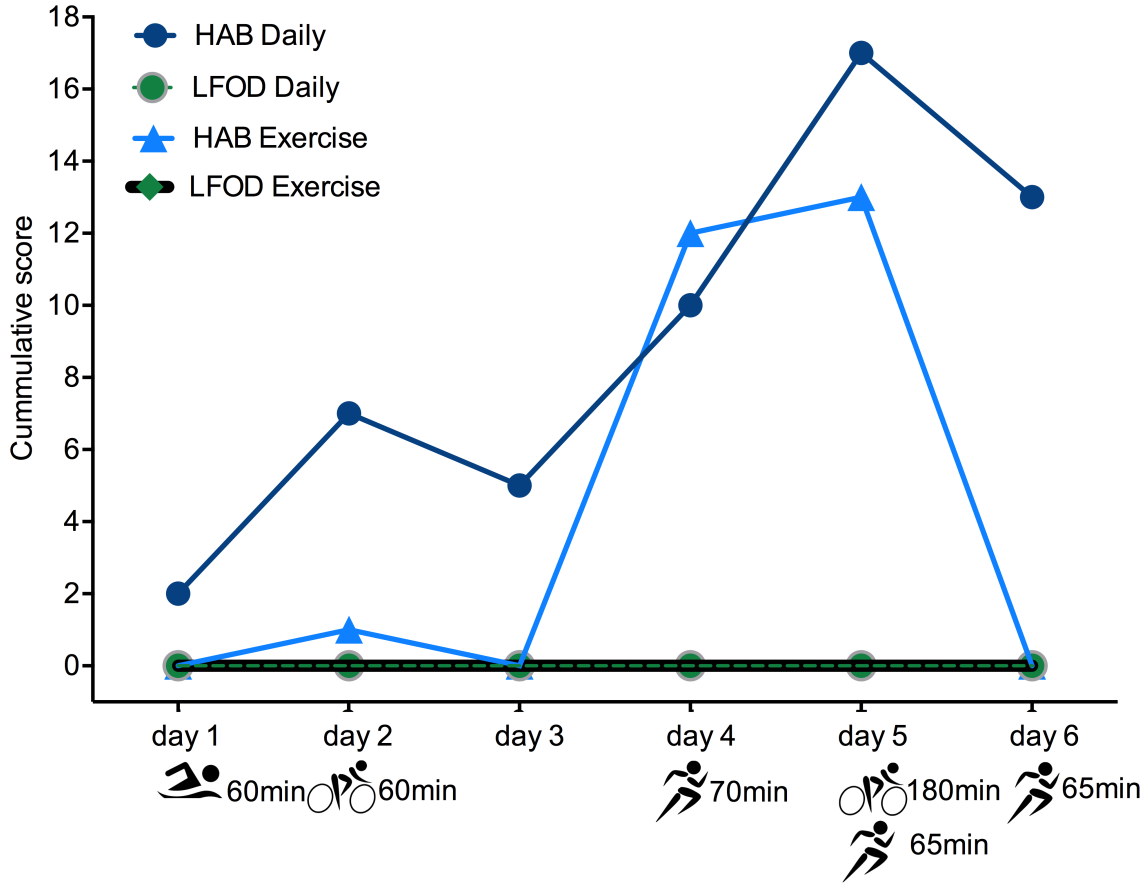

Figure 5.2 – Cumulative Daily GI symptoms scores; HAB=habitual, LFOD=low FODMAP.

5.6 Reflections

Many endurance athletes who struggle with persistent exercise-induced GI distress fail to resolve these potentially debilitating symptoms through commonly recommended dietary approaches. Although a subjective measure, GI symptoms have the potential to negatively impact performance (77) and thus it may be important to assess even lower severity symptoms (<3), particularly at the elite level where very small changes can have important performance impacts (71). Athletes and some practitioners believe that interventions such as low-residue or GFDs will improve GI issues (39, 97). GFDs are naturally low in fructan and GOS, and may actually be the modulating factors in reported symptom improvement and not gluten itself (52). However, the athlete in this case study indicated no improvement with a previous GFD. Instead

the results suggest a low FODMAP intervention as a potentially novel approach to improve GI symptoms occurring with strenuous exercise, where the gut is compromised (167).

Through this case study, we are unable to identify whether an individual FODMAP or a combination of foods rich in FODMAPs were responsible for the GI distress reported by the athlete during the habitual diet. The habitual diet was extremely high in lactose and lactose may be a primary trigger, however, the athlete had not reported lactose intolerance. In an athletic population it is important to note that lactose intakes may be greater than the general population (8, 64) due to heavy dependence on dairy as a source of high quality protein and to replace sweat calcium loses (60). Reliance on dairy protein has also been shown to support an increase or maintenance of lean body mass and support bone collagen formation during period of energy restriction (81) which many endurance athletes engage in to improve power to weight ratio. In conjunction with a short-term low FODMAP diet before races or key running training sessions, self-administration of low doses of lactose containing foods (e.g. ½ cup of cow's milk) were subsequently recommended assess tolerance.

Several factors should be considered with the implementation of a low FODMAP dietary approach in athletes pertaining to assessment, counselling strategies and execution of the diet. Counselling strategies that curtail a "placebo effect" are integral to measuring real symptom change and the magnitude of change verses the influence of the belief in an intervention (10). Prior to implementing a low FODMAP diet, integration of appropriate dietetic and medical practitioners is imperative, particularly with severe or persistent cases of GI distress, to rule out functional GI disorders and other triggers (e.g. nutritional, physiological or psychological). Similarly, a low FODMAP diet for athletes should be administered by a dietitian experienced in sport nutrition and low FODMAP diet administration. This intervention is also best tested in the off-season and trialled under conditions where symptoms occur. For athletes that respond

positivity to a low FODMAP diet the intervention length should be minimized to reduce unnecessary dietary restriction. Food choice is key to the successful implementation of low FODMAPs diet as it has the potential to be lower in prebiotics, which may influence the microbiome composition (174). Limited research regarding the nutritional adequacy of a low FODMAP diet and long-term effects raises concern surrounding the nutritional suitability of this diet, especially for athletes, if appropriate variety and quantity is not integrated (153). An objective of the intervention should also include identifying, via strategic re-introduction of foods, specific high FODMAP foods that trigger symptoms, as not all FODMAPs may be culprits. Therefore, our recommendation to the athlete was to follow a low FODMAP diet 2 to 3 days before events or critical training sessions to alleviate symptoms, namely; bloating, intestinal cramps, flatulence, urge to defecate.

Psychological stresses also conceivably influence GI symptoms and were therefore additionally monitored. DALDA responses of 'worse than normal' were higher during the habitual dietary period alongside more severe GI symptoms compared to the low FODMAP period, plausibly indicating a perceived reduction in gut distress. Several studies have found unique gut-brain axis relations associating psychological stress with increased GI disorders and symptoms (12, 84, 158). The reverse may also occur, as psychological stress levels are likely to increase with GI symptoms, especially in competitive situations. Therefore, monitoring stress triggers and stress response should correspondingly be part of an athlete nutrition plan relating to GI distress.

Overall, a reduced FODMAP diet led to a successful resolution of GI symptoms that were predominantly triggered during running for the athlete. These results provide a foundation and practical approach to initiate extended research investigating the effects of FODMAPs in athletes with persistent exercise-induced GI symptoms.

Chapter 6: A preliminary study of FODMAP modulation as a novel strategy to reduce gastrointestinal distress in athletes

6.1 Rationale

Measurable GI symptom improvements reported in the low FODMAP case study intervention (Chapter 5), alongside the quantification of FODMAP elimination among athletes (Chapter 4), underpin the rationale for an intervention study assessing the effects of this diet in a larger athlete cohort with GI distress. As a preliminary investigation of the efficacy of a low FODMAP diet in healthy athletes with GI distress a single-blinded randomized, crossover dietary intervention of a high versus low FODMAP diet was executed. In this study, healthy runners with self-reported GI distress adhered to either a low or high FODMAP diet in a single-blinded crossover design. While controlling and replicating diet and exercise, GI symptoms and psychological wellbeing were evaluated. As a preliminary yet foundational study, the results suggest FODMAP modification may be a promising sport nutrition strategy to reduce GI symptoms in some athletes. This chapter has been submitted and is under review.

6.2 Abstract

Purpose: Gastrointestinal (GI) distress in endurance athletes is prevalent and detrimental to performance. Adverse GI symptomatology can be analogous with irritable bowel syndrome, where fermentable oligosaccharide, disaccharide, monosaccharide and polyols (FODMAP) reduction has demonstrated efficacy. This study investigated a low FODMAP (LFOD) diet on GI distress parameters in runners with a history of non-clinical exercise-associated GI symptoms. **Methods:** Eleven recreationally competitive runners (5 males, 6 females; 5km personal best 23:00±4:02 min:sec) participated in the study. Runners were allocated to a randomized 6-day LFOD or high FODMAP (HFOD) diet separated by a 1-day wash-out in a controlled, single-blinded crossover study. In each period participants completed strenuous running sessions consisting of 5x1000m interval (day 4) and a 7km threshold run (day 5). GI symptoms (during-exercise and daily) and the Daily Analysis of Life Demand for Athletes (DALDA) questionnaires were completed. Area under the curve (AUC) was calculated for daily GI symptoms across each dietary period and analysis was conducted using multilevel mixed-effects linear regression for comparison between the two diets. **Results:** A significantly smaller AUC for daily GI symptoms.6-days^{-1} during the LFOD compared to HFOD (mean difference -13.4, 95% CI [-22, -4.60], P=0.003) was observed. The specific GI symptoms significantly lower during LFOD were flatulence (P<0.001), urge to defecate (P=0.04), loose stool (P=0.03) and diarrhoea (P=0.004). No significant differences in during exercise symptoms or DALDA responses were observed between diets (P>0.05). **Conclusion:** Preliminary findings suggest that short-term FODMAP reduction may be an intervention to minimize daily GI symptoms in runners with exercise-related GI distress.

6.3 Introduction

Optimal athletic performance can be directly compromised by gastrointestinal (GI) dysfunction. High rates of GI distress are reported to occur in 30-50% of endurance athletes (39, 52). Although most symptoms occurring are mild to moderate, severe symptoms may impair training capacity and performance (39). During strenuous exercise GI symptoms are triggered in part by significant splanchnic hypoperfusion, as blood is shunted away from the GI tract towards the working muscles, which instigates acute enterocyte injury, increased intestinal permeability and altered motility (167). Symptoms associated with exercise-induced GI distress are numerous, but many are analogous with clinical indications associated with irritable bowel syndrome (IBS) (55, 148, 167). In particular, lower abdominal symptoms such as diarrhoea, bloating, abdominal pain and flatulence share remarkable similarities in both conditions. Interestingly, fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) restriction has been emerging as an efficacious treatment for IBS symptoms (34, 54, 148). Therefore, it is plausible that FODMAP manipulation may also positively affect exercise-associated GI symptoms (64, 152).

Nutritionists and athletes employ various dietary strategies to reduce exercise-associated GI distress, including limiting dietary fibre and lactose, eating low-residue foods around competition, training the gut to tolerate larger carbohydrate loads or removing gluten (35, 37). A gluten-free diet has become a popular regimen to supposedly alleviate exercise-associated in noncoeliac athletes (98) and IBS-related GI symptoms (16) although negligible peer-reviewed evidence exists supporting these anecdotal claims (98). Conversely, data in non-athlete clinical populations propose that GI symptom improvement associated with gluten elimination may actually be modulated by the subsequent reduction in FODMAP content that generally accompanies a gluten-free diet, and not necessarily gluten elimination itself (52, 118). A low FODMAP diet is predicted to be the next popular equivalent to the gluten-free diet

(41).

FODMAPs are poorly absorbed short chain carbohydrates that have been shown to increase osmotic load in the small intestine and colonic gas volume, which instigates adverse symptoms in hypersensitive individuals (152). Examples of foods restricted with a low FODMAP diet include: lactose-containing products such as cow's milk, a range of fruit high in fructose, wheat-based products, onions and garlic encompassing fructans and galactooligosaccharides, and fruits with stones (pits) or confectionary with naturally occurring or added polyols. In Western diets up to 40 g of undigested carbohydrates reach the colon daily including an average of 1-10 $g.day^{-1}$ of inulin and oligofructans (166). In sensitive individuals, FODMAPs can cause adverse GI symptoms. FODMAPs are also important dietary constituents offering favourable prebiotic effects such as acting as a substrate for beneficial microbial populations, increasing stool bulk, enhancing micronutrient absorption and immune function (104), so unnecessary restriction is not advocated. To date, studies suggest that healthy individuals without IBS would not benefit from restricting FODMAP intake (64, 123) and a prolonged strict low FODMAP diet does not appear to be a common practise amongst athletes (95). However, in athletes looking to reduce GI symptoms self-reported data indicates that over half eliminate high FODMAP foods, without necessarily realizing that these foods were considered part of the FODMAP family (95). Up to 88% of these athletes report subsequent symptom improvement (95). Therefore, it is plausible that the physiological mechanisms and symptoms associated with exercise-associated GI injury increase sensitivity to all, or some FODMAPs, and it is relevant to consider if symptoms could be reduced with FODMAP restriction in endurance athletes.

We have recently published a case study showing positive outcomes of a low FODMAP dietary intervention in a multisport athlete (94). Based on these results, and encouraging clinical

research on low FODMAP diets (152), it is imperative that the manipulation of short-chain carbohydrate be investigated as a novel tool for individualized dietary management aimed at attenuating GI distress in a group of healthy athletes. Hence, the aim of this preliminary study was to examine the effect of a low FODMAP versus a high FODMAP diet on symptoms of self-reported GI distress and perceived wellbeing in recreationally competitive runners with a history of GI symptoms. Our *a priori* hypothesis was that a short-term low FODMAP diet would reduce the severity of GI symptoms appearing daily and during strenuous running sessions.

6.4 Methods

6.4.1 Participants

Eleven recreational competitive runners (>25 km running per week) aged 18-50 years with self-reported persistent exercise-associated GI symptoms were invited to participate in this study. Inclusion criteria included: a minimum of three chronic GI symptoms (e.g. nausea, bloating, diarrhoea) with score greater than 4 (quite often) on the background GI questionnaire (131), a habitual high FODMAP intake of ≥20 g FODMAP.day^{-1} (62) as assessed with the Complete Nutrition Assessment Questionnaire (CNAQ; http://www.cnaq.com.au/) (8) and the capacity to complete two consecutive days of prescribed strenuous running training during the study. Exclusion criteria included: a history of food intolerance (e.g. diagnosed lactose intolerance), known coeliac disease or known familial history of coeliac disease, clinically diagnosed noncoeliac gluten sensitivity or IBS, current adherence to any special diet, or any pre-existing medical condition that could be affected by dietary intervention. Ethics approval was obtained from the Tasmanian Health and Medical Human Research Ethics Committee (H0015151). All participants provided signed informed consent.

6.4.2 Experimental Design

Utilizing a single-blind, crossover design participants were randomized to receive either a high FODMAP (HFOD) or a low FODMAP (LFOD) diet for 6-days, separated by a 1-day washout (28), followed by the alternative diet (**Figure 6.1**). Randomization was generated using GraphPad QuickCals software. Participants were informed that they would be assigned "*Specific Carbohydrate Diet A* or *B"* for the first dietary period then the alternate diet for the subsequent dietary period, with no specific reference to FODMAPs or gluten. Participants self-selected their training schedule based on study guidelines (see details below). All training was replicated during the subsequent dietary period. Participants were asked to record their daily exercise, food intake and complete a post-exercise GI questionnaire, daily GI questionnaire and Daily Analysis of Life Demands (DALDA) questionnaire each day throughout the two dietary periods.

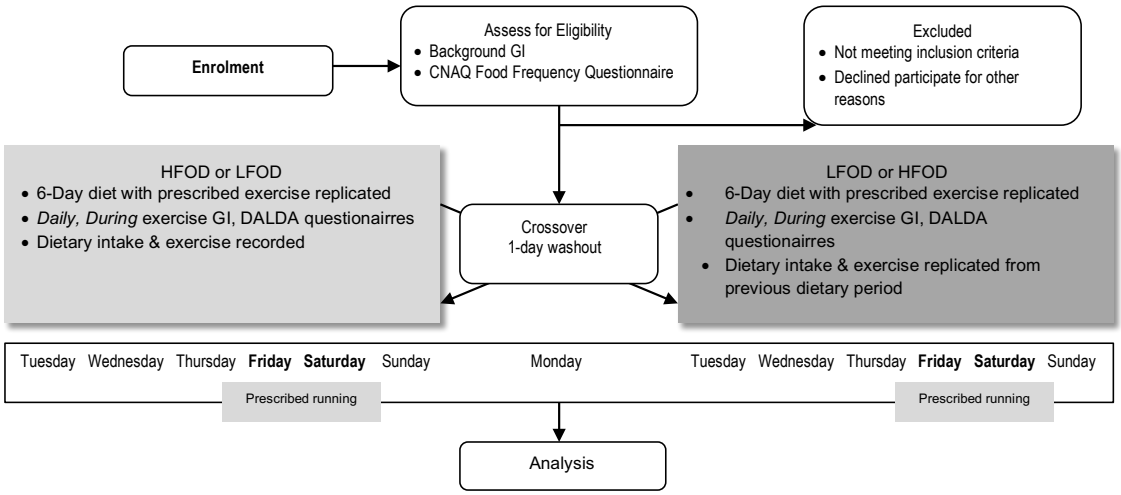

Figure 6.1 Schematic showing participant selection and study design. LFOD=Low FODMAP diet, HFOD=High FODMAP diet, GI=gastrointestinal, DALDA=Daily Analysis of Life Demands for Athletes.

Food Preparation & Provision: Participants were provided with pre-made frozen lunch and dinner meals (prepared, weighed and frozen in a commercial kitchen; Matson's Catering, Launceston, Australia), breakfast (cereals, breads, milk, yoghurt) and snack foods (muesli bars, crackers). As the study participants were blinded, all food was packaged in the same opaque containers and labelled according to each dietary period (e.g. week-1 muesli bars, day-2 lunch). Alongside the controlled study food provisions, the participants were able to self-select from a suggested list (of *choose* and *avoid*) and supplement the study food with fresh fruits, vegetables and nuts with the stipulation that a counterpart substitution be exchanged in the second dietary period. A registered dietitian (lead researcher) provided dietary education to participants on nutrition intake recording and appropriate food selections. LFOD and HFOD meals were established based on previous research (123), Monash University's low FODMAP diet resources (http://www.med.monash.edu/cecs/gastro/fodmap/) and typical athlete diets (21). Recipes for LFOD and HFOD were similar, but ingredients modified to alter the FODMAP content (**Table 6.1**). Meals were matched for content of total energy, protein, carbohydrate, fat and fibre; however, resistant starch information was not available due to the absence of comprehensive resistant starch food composition tables. Each meal was analysed for FODMAP content using a FODMAP specific database (FoodWorks Professional 7, Xyris, Brisbane, Australia) to ensure that LFOD meals contained less <0.5 g FODMAP.meal^{-1} (63). An example of the study meals for each diet are provided in **Table 6.1**. The prototype study menu presented a macronutrient profile containing carbohydrate 5-7 g.kg^{-1}, protein 1.2-1.7 g.kg^{-1} and fat 0.8-1.2 g.kg^{-1} (107) (FoodWorks Professional 7, Xyris, Brisbane, Australia).

Table 6.1 Example of high and low FODMAP diets

Meal	Low FODMAP diet	High FODMAP diet
Breakfast	low FODMAP muesli[a]	muesli with dried fruit and nuts
	lactose-free milk	milk
	blueberries	apple
	coffee/tea with lactose-free milk	coffee/tea with milk
Snack	corn Cruskits	rye Cruskits
	lactose-free yogurt	yogurt
	grapes	nectarine
Lunch	maple glazed salmon on quinoa/rice pesto pasta[b]	honey glazed salmon on durum wheat pest pasta[c]
Snack	gluten-free biscuits	wheat biscuits
	cheddar cheese	cheddar cheese
	tomato, cucumber	snap peas, cucumber
Dinner	grilled chicken and vegetables on quinoa[d]	grilled chicken and vegetables on couscous[e]
Snack	lactose-free yogurt	yogurt
	strawberries	cantaloupe
	coffee/tea with lactose-free milk	coffee/tea with milk

[a] low FODMAP muesli made with rice crispies, corn flakes, quinoa flakes, shredded coconut, and pumpkin seeds

[b] low FODMAP pesto pasta made with: cherry tomatoes, eggplant, garlic infused oil, pine nuts, basil, parsley

[c] high FODMAP pesto pasta made with: cauliflower, asparagus, pistachios nuts, basil, parsley, garlic

[d] low FODMAP vegetables included: small portion sweet potato, red bell pepper, spinach

[e] high FODMAP vegetables included: larger portion of sweet potato, beetroot, garlic, red onion

Exercise and Prescribed Running: Participants self-selected their training schedule based on study guidelines which indicated: day 1 and 2 to be light to moderate intensity training, day 3 to be rest or very light non-running exercise (e.g. yoga, swimming). Day 4 and 5 were prescribed very intense running sessions and day 6 was entirely self-selected exercise or rest. Day 4 (interval session) consisted of a 10-minute self-prescribed warm up with increasing intensity, 5 x 1000 m interval pace (100% of predicted $v\dot{V}O_{2max}$) with 3-minute brisk walk or

light jog between intervals followed by a 10-minute self-selected cool down. Day 5 (threshold session) consisted of a 7 to 10-minute self-selected warm up with increasing intensity, 7 km at threshold pace (~90% of predicted $v\dot{V}O_{2max}$) followed by a 10-minute self-selected cool down. Prescribed running sessions were individually monitored using participants' personal Garmin GPS running watches (Forerunner® 735XT, 630XT, 235 or 910XT) and all training was replicated in the second intervention period. Interval and threshold paces were individually prescribed based on calculations from a recent race performance using VDOT (velocity at $v\dot{V}O_{2max}$) tables (33). Running sessions were completed on flat terrain, at the same time of day (±30 min) over the period of data collection (December 2015 to February 2016).

Gastrointestinal Symptom Monitoring: During-exercise GI questionnaires and daily GI questionnaires were used to assess the occurrence and severity of upper and lower abdominal symptoms determined using a 10-point scale ranging from 0 "no problem at all" to 9 ''the worst it has ever been" (131). Section 1 of the questionnaire addresses upper abdominal symptoms: reflux, heartburn, burping, bloating, stomach pain/cramps, vomiting and nausea. Section 2 addresses lower abdominal symptoms: flatulence, urge to defecate, left abdominal pain (side stitch), right abdominal pain (side stitch), loose stool, diarrhoea and intestinal bleeding (131). Participants completed the during-exercise GI questionnaire immediately following their training session and the daily GI questionnaire at the end of each day at the same time. GI symptom scores were tabulated for each day and exercise session (131). Mean scores for daily GI symptoms, during-exercise GI symptoms, and incremental area under the curve (AUC) for daily GI symptoms across all 6-days of each dietary period were compared between the diets.

Perceptual Wellbeing Monitoring: Participants completed the DALDA questionnaire at the end of each day. This questionnaire is used to assess general stress levels (Part A) and to

determine stress-reaction symptoms (Part B) (139) using a rating scheme of "worse than normal," "normal," or "better than normal" for variables. Scores were tabulated and the "worse than normal" and "better than normal" scores compared between the two dietary periods.

6.4.3 Statistical Analysis

All GI symptoms and DALDA scores and dietary variables were treated as continuous data (129)and compared between the two diets using multilevel mixed-effects repeated measure linear regression adjusted for order and period effects (Stata 13.0, StataCorp LP, College Station, TX). Regression residuals were tested for assumptions of linear regression (heteroscedasticity, skewness, kurtosis or linearity). Where regression residuals did not meet the assumptions of linear regression the analyses were repeated with multilevel mixed-effects ordered logistic regression. For consistency, all comparison results are presented as mean difference (95% Confidence Interval). For each dietary intake variable, the mean±SD was calculated and compared between the diets using mixed-effects ordered logistic regression. P values ($P<0.05$) are from the relevant analyses (linear regression or ordered logistics regression in case of violation of linear regression assumptions). Incremental AUC, above zero, for daily GI symptoms was calculated from total daily GI symptom scores over each 6-day diet (GraphPad Prism, version 6.0, San Diego, CA) and compared between the two diets.

6.4 Results

6.4.1 Participants details and compliance

Dietary intake (**Table 6.2**), GI symptom assessment (**Figure 6.2**) and DALDA results were available for 11 of 12 participants (5 males, 6 females, 41±10 years, weight 69.0±12.0 kg, height 171.1±10.0 cm, 5 km personal best 23:00±04:02 min:sec). One participant was removed due to incomplete data. Background GI symptoms, primarily boating, flatulence, urge to defecate and loose stool were predominant and were reported to occur *quite often* to *always* (score of ≥4 to 9). Total habitual FODMAP intake was 43.8±16.9 g FODMAPs.day^{-1}. The prescribed running sessions were completed as assigned, and exercise volume matched in each period (HFOD total exercise volume 50:12:43 hh:min:sec, 0:56:51±0:25:33 daily mean±SD; LFOD 50:36:42, 0:57:18±0:23:55) with no significant differences in temperature (16.2±5.2 vs 15.7±4.9°C) or humidity (64.0±14.9 vs 55.3±19.6%) for the LFOD or HFOD dietary periods, respectively. No order or period effects were found for total daily GI symptoms, during-exercise GI symptoms or DALDA on any of analysed variables except for loose stool (mean difference -0.35, 95% CI [-0.79, -0.01], P=0.03).

All participants consumed the prescribed diets and dietary intake was analysed from food intake records for HFOD and LFOD. The composition of the diets is shown in **Table 6.2**. The two test diets were similarly matched for total energy, carbohydrate, and fibre. Protein and fat were statistically different between the diets (P=0.03 and P=0.003, respectively). These differences are of negligible clinical significance given the 5g protein and 7g fat daily variances. As designed, FODMAP intake differed significantly between the two diets being 41.4±7.9 g.day^{-1} HFOD and 8.1±3.5 g.day^{-1} LFOD (P<0.0001).

Table 6.2 Composition of dietary intake during the habitual and low FODMAP dietary periods

Dietary Component	HFOD	LFOD	P value
Total energy (kcal)	3181 ± 403	3198 ±429	0.724
Total carbohydrate (g)	323 ± 63	327 ± 67	0.569
Total protein (g)	158 ± 16	153 ± 20	0.030*
Fat (g)	130 ± 12	137 ± 15	0.003*
Fibre (g)	32 ± 5	30 ± 5	0.318
Total FODMAPs (g)	41.4 ± 7.9	8.1 ± 3.5	<0.0001*
Excess fructose (g)	1.9 ± 0.54	0.5 ± 0.4	<0.0001*
Lactose (g)	28.0 ± 8.6	0.9 ± 0.3	<0.0001*
Total oligosaccharides (g)	8.7 ± 1.9	5.5 ± 3.2	0.001*
Fructooligosaccarides (g)	7.3 ± 1.8	4.5 ± 2.7	<0.001*
Galactooligosaccarides (g)	1.4 ± 0.3	1.0 ± 0.5	0.006*
Total Polyols (g)	2.9 ± 0.9	1.3 ± 0.7	<0.0001*
Sorbitol (g)	1.8 ± 0.9	0.9 ± 0.4	0.001*
Mannitol (g)	1.1 ± 0.3	0.4 ± 0.5	<0.0001*

Energy, macronutrients and fibre were calculated using FoodWorks dietary software, which is based on the Australian Food Composition tables. Total FODMAPs = excess fructose + lactose + sorbitol + mannitol + fructans + galactooligosaccharides (GOS). Bold text indicates additive constituents for total FODMAPs.

Data is presented as group (n=11) mean ± standard deviation (SD) for HFOD and LFOD.

*Significance between HFOD and LFOD (P<0.05).

6.4.2 Gastrointestinal Symptoms: Daily and During Exercise

Daily GI symptoms scores were collected each day of the study and tabulated. Individual AUC responses show that 82.0% (9 of 11) of participants had a smaller AUC for daily GI symptom scores.6-days^{-1} during the LFOD compared to HFOD (mean difference -13.4, 95% CI [-22, -4.60], P=0.003; **Figure 6.2a**). The group AUC (**Figure 6.2b**) was lower in LFOD (31.4±24.6; mean±SD) compared to HFOD (44.6±33.6). Specific daily GI symptoms that were reduced during LFOD included: flatulence (mean difference -1.12 95% CI [-1.55, -0.75], P<0.001), urge to defecate (mean difference -0.41, 95% CI [-0.81, -0.02], P=0.04), loose stool (mean difference -0.38, 95% CI [-0.73, -0.04], P=0.03) and diarrhoea (mean difference -0.45, 95% CI

[-0.75, -0.14], P=0.004). The mean GI symptoms scores for day 1 to 6 were higher during HFOD compared to LFOD (mean difference -2.45, 95% CI [-4.21, -0.69], P=0.006; **Figure 6.2c**).

During-exercise GI symptoms scores for the HFOD and LFOD dietary periods for day 4 and day 5, when prescribed strenuous running sessions, were compared. Half of the participants rated GI symptoms during the prescribed running sessions to be moderate to severe (≥3). Burping was the one symptom that was significantly higher (mean difference 0.30, 95% CI [0.01, 0.58], P=0.04) during LFOD compared to HFOD. No significant differences in any other GI symptoms were found during the prescribed running sessions between HFOD and LFOD.

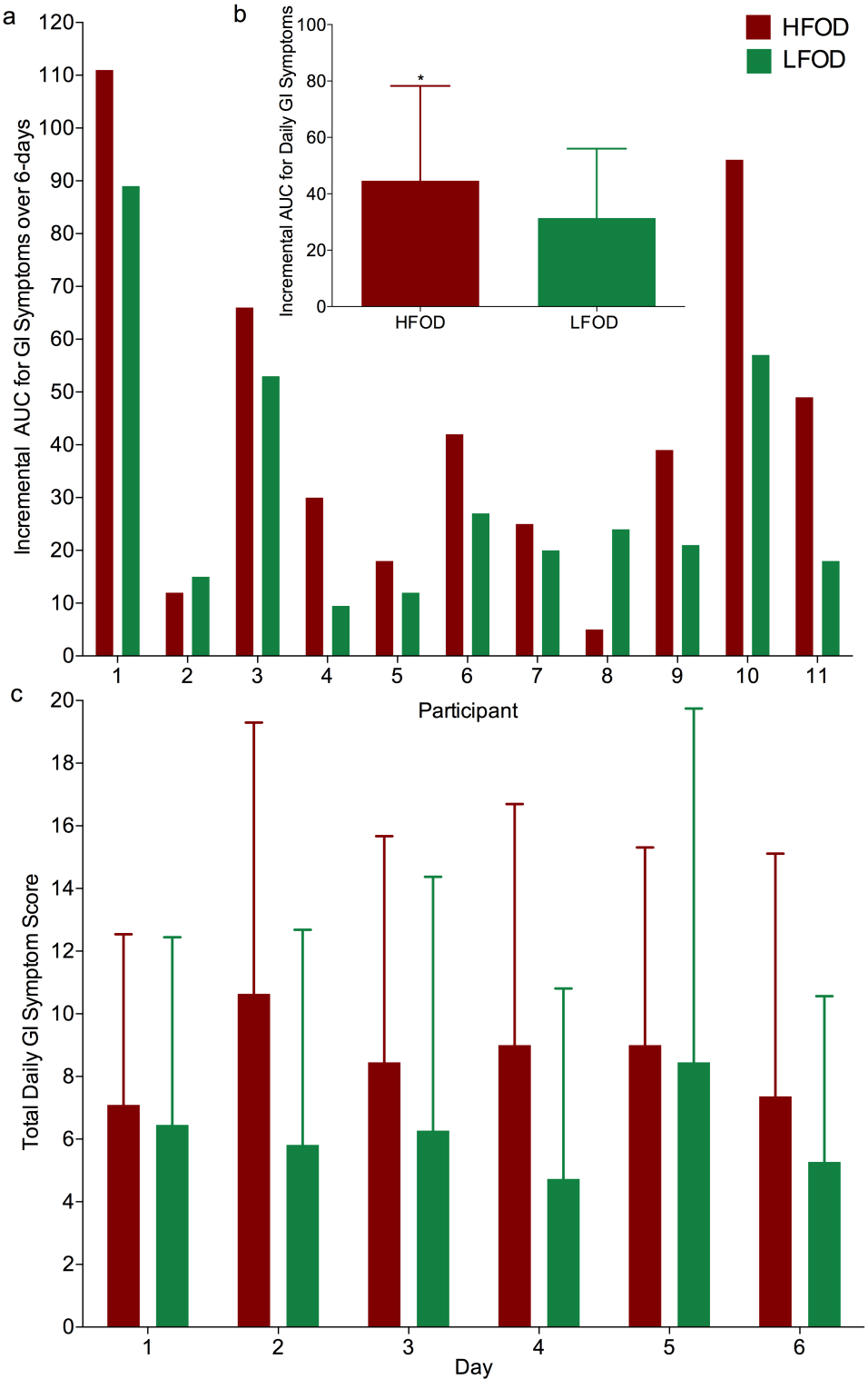

Figure 6.2 – (a) Individual area under the curve (AUC) for daily gastrointestinal (GI) symptom scores over 6-days for LFOD vs HFOD (n=11). (b) Mean group AUC during LFOD compared to HFOD for daily GI symptom scores. (c) Mean total daily GI symptom scores for each day (day 1-6) of the dietary period for all participants (error bars represent standard deviations) on LFOD and HFOD (P=0.006); * Denotes significance (P=0.003).

6.4.3 Perceptual Wellbeing

Overall wellbeing was measured using DALDA and the worse and better than normal scores were compared for each dietary period, as well as the scores on the prescribed training days (day 4 and 5). Total worse than normal scores for stress (part A) and stress response (part B) combined were not different (mean difference -0.45, 95% CI [-1.30, 0.40], P=0.30) during HFOD (3.71±3.18) compared to LFOD (3.30±3.31). Similarly, total better than normal scores for the HFOD (2.59±2.80) and LFOD (2.97±3.66) were not significantly different across each dietary period (mean difference 0.43, 95% CI [-0.52, 1.37], P=0.38). Total worse than normal scores on day 4 or day 5 were not different (mean difference -0.82, 95% CI [-2.26, 0.63], P=0.30; mean difference -0.91, 95% CI [-2.35, 0.53], P=0.25, respectively). Total better than normal scores on day 4 or day 5 were not different (mean difference 0.5, 95% CI [-1.11, 2.11], P=0.55; mean difference 1.23, 95% CI [-0.39, 2.84], P=0.10, respectively).

6.5 Discussion

Dietary intake, and its interactions with strenuous exercise, are of particular importance to athletes as resulting GI distress is a common problem potentially impairing training capacity and performance (37). This is the first study to examine the effects of a short-term low FODMAP diet on GI symptoms and perceptual wellbeing in athletes with a history of exercise-associated GI distress. The aim of this preliminary study was to investigate if self-reported and case-study outcomes, demonstrating beneficial effects of FODMAP reduction on exercise-associated GI symptoms (94, 95), could be substantiated in a larger cohort. Results from this preliminary study indicate that a low FODMAP diet had a positive effect on daily GI symptoms in 82% of participants.

6.5.1 Effect of low FODMAPs on daily GI symptoms

In participants with persistent exercise-associated GI symptoms, 9 of the 11 reported a reduction in daily GI symptoms on a short-term low FODMAP diet (**Figure 6.2**). To date, low

FODMAP diet research has predominantly focused on clinical populations, specifically individuals with IBS. Discernible symptomatic improvements in approximately 70% of IBS patients encourage the use of this diet as first line treatment (152). A limited number of investigations have included healthy controls (64, 116, 123) and results suggest that although healthy individuals demonstrate functional changes with FODMAP ingestion, GI symptoms remain very minor or non-existent (116, 123). Low level GI symptoms likely have a negligible impact on athletic performance, but more moderate to severe symptoms may be detrimental (55). Although healthy populations, including healthy athletes, would not be hypothesized to benefit from FODMAP reduction with reduced GI symptoms, it is interesting to consider if the unique physiological, mechanical and nutritional stress encountered by endurance athletes (38, 168) could increase susceptibility to any dietary triggers, such as FODMAPs, for some of these athletes. GI symptoms are largely variable but our preliminary data suggests that a short-term low FODMAP diet may be efficacious in the management of daily GI symptoms (**Figure 6.2**); particularly lower abdominal GI symptoms, in healthy athletes. Although no difference in GI symptoms were observed during exercise, the ability to reduce daily GI symptoms would be very advantageous in extended events like the Tour de France, rigorous training camps or multi-event athletics, which feature sequential days of intensive and extensive exercise.

6.5.2 Effect of low FODMAPS on exercise specific GI symptoms

GI symptoms during prescribed running sessions were similar for the HFOD and LFOD dietary periods. In race conditions 4–32% of athletes report GI distress and some symptoms are so severe that withdrawal from competition results (131). Numerous factors exacerbate GI symptoms during exercise including mechanical impact, physiological stress and dietary intake. Significantly greater GI issues are reported during prolonged events (e.g. Ironman), as compared to relatively shorter events, such as the marathon (131). Ingestion of carbohydrates as consumed in endurance sport, particularly solutions with a high osmolality, are associated

with the development of GI symptoms during exercise (130, 136). Exercise duration in the current study did not warrant carbohydrate ingestion (75), however it is interesting to consider if ingestion of short-chain carbohydrates during exercise or pre-existing FODMAPs in the GI tract would have additive osmotic actions and consequent symptoms (39, 159). It is likely that the chosen exercise duration (45-60 $min.day^{-1}$), coupled with no CHO ingestion during exercise, curtailed any measurable difference in during exercise GI symptoms between the diets. Although this study did not investigate mechanistic hypotheses it may be conceivable that GI symptoms during exercise could be exacerbated with the presence or during exercise intake of FODMAPs. In general GI symptom reduction, our preliminary findings do support further research of the hypothesis that FODMAP reduction would positively affect the severity or occurrence of exercise-associated GI symptoms.

6.5.3 Effects of altering FODMAPS on perceptual wellbeing

Extreme and persistently high chronic training loads are associated with greater psychosomatic stress. Psychological wellbeing, personality traits and psychosocial factors, such as stress, also have the potential to influence perceptions of GI symptom presence and severity (84, 108). The reverse may also occur, in that GI symptoms caused by exercise may be reflected by reductions in overall perceptual wellbeing. In the current study DALDA evaluation was conducted alongside each dietary intervention with the aim to capture the relationship between perceptual wellbeing and GI symptoms influenced by diet and exercise stress. In athletes, the multifactorial nature of GI distress is well known and the influence of psychological wellbeing or stress on alterations of the autonomic nervous system has been recognized (83, 158). These changes in homeostatic balance have been characterized by slowing of gastric emptying, increased distal colonic motility and acceleration of intestinal transit, further contributing to adverse GI symptoms (20). In the present study, it is possible that DALDA was not a sensitive

enough tool to detect any FODMAP related changes. A more chronic fatigue state over several days/week or longer is likely required to capture changes in DALDA responses (1, 65).

6.5.4 Reflections for future studies

Dietary control was achieved; however, three reasons are suggested as to why no difference in GI symptoms were observed during the prescribed strenuous running sessions. First, daily GI symptoms on the LFOD diet were lower compared to HFOD. Lower pre-exercise symptomology during the LFOD may have skewed perceptions of the during exercise GI symptoms toward being more exaggerated (greater net difference) resulting in reporting of higher during exercise symptom scores for LFOD. Secondly, although residual FODMAPs are suggested to transit through the GI tract in less than 3-days (35) a longer period of LFOD may be necessary to augment further symptom reduction. Changes in the gut microbiome occur over time as the biomass evolves and it is possible that the full benefits of the diet are not realized until 7-days (62) or a few weeks (152). Most importantly, exercise duration has been correlated with GI distress (131) and longer running sessions may be required to distinguish differences in GI symptoms between the diets. A greater effect may be observed under more extreme exercise conditions and future research should consider this element in the methodology.

6.5.5 FODMAP manipulation considerations for the practitioner

Our developing work proposes that FODMAP manipulation may be an innovative addition to the sport nutrition practitioners' toolbox for management of exercise-associated GI distress. Certain considerations must be considered when trialling short-chain carbohydrate restriction with athletes as dietary requirements are individual and unnecessary food restriction may compromise optimal fuelling (114). When appropriately planned, under the guidance of a dietetic professional, a low FODMAP diet can be matched for energy, macronutrients and fibre

(**Table 6.2**). Although differences in protein and fat intake were statistically significant between LFOD and HFOD, 7 and 5 g, respectively, these findings are not clinically significant. As a source of high quality protein, cow-based dairy is often consumed at or above the general population recommendation of two to four servings per day(24). Coinciding high lactose intakes are likely (**Table 6.2**) and should be investigated as a primary trigger for GI symptoms with appropriate high protein substitutes made, such as lactose free milk. A low FODMAP diet should be considered once typical GI symptom triggers have first been assessed, such as lactose (35, 37).

Intakes of prebiotic fructooligosaccharides and galactooligosaccharides, found in high amounts in wheat and legumes, are restricted with a low FODMAP diet, which is concerning. These prebiotics stimulate healthy colonic Bifidobacterium. After 4-weeks of a restricted fermentable carbohydrate diet Bifidobacteria populations were decreased in IBS patients (153). Immune health may be compromised with lower Bifidobacterium count, which is an important consideration for overall athlete immunity and health (57). In athletes, it is unclear if risk associated with decreased healthy bacterial populations due to diet may be more or less apparent as exercise further alters diet-microbe-host metabolic interactions and may support higher gut microorganisms diversity (29, 122). Exercise and an athletes' diet could offer a protective element against a decrease in healthy gut bacterial populations associated with FODMAP restriction. Given the restrictive nature and novelty of this dietary approach a systematic and individualized approach will be obligatory for successful and efficacious implementation of a low FODMAP diet in an athletic setting.

6.5.7 Conclusions

Results from this study have shown that a short-term LFOD results in significantly lower daily GI symptoms over the intervention period compared to a HFOD diet in athletes with a self-

reported history of persistent exercise-associated GI distress. Exercise-associated GI distress and pathophysiology of IBS are multifactorial, but both conditions feature similar symptomatology. Although, more work is needed to determine the effectiveness of a low FODMAP diet, our preliminary findings suggest this dietary approach may be applicable beyond the clinical realm and offer a novel strategy to reduce GI symptoms in some symptomatic but clinically healthy athletes.

Chapter 7: Commercial hype vs. reality: Our current scientific understanding of gluten and athletic performance

This chapter has been published in Current Sports Medicine Reports as an invited review and appears as:

Lis DM, Fell JW, Ahuja KD, Kitic CM, Stellingwerff T. Commercial hype versus Reality: Our current scientific understanding of gluten and athletic performance. *Curr Sports Med Rep.* 2016;15(4):262-8.

Thompson Reuters journal impact factor: 1.336
SJR journal ranking: Q3
Altmetrics score: 32

7.1 Rationale

Rapid explosion in the gluten-free market alongside an extraordinary high uptake of GFDs amongst NCA has far outpaced evidence-based research in this area. Upon commencement of my PhD investigations NCA had already rapidly been adopting a gluten-free lifestyle with no evidence base supporting the purported beneficial effects of this diet for athletes not clinically requiring gluten-avoidance. Due to the paucity of evidence-based research investigating the effects of GFDs or FODMAP manipulation in clinically healthy athletes Chapter 7 is presented as a review of the literature towards the end of my thesis document and includes my seminal work in this area. This invited and published review provides an overview of the clinical conditions in which a GFD is required followed by a description of the rationale, beliefs and experiences pertaining to GFD for NCA. Athlete perceptions and dietary behaviours are examined alongside evidence-based research. Lastly, other confounding dietary factors, a belief effect and the role of FODMAPs are examined. This literature review underpins the

focus and application of this thesis to determine the effects of a GFD or low FODMAP diet in clinically healthy NCA.

7.2 Abstract

Recent explosion in the prevalence of gluten-free athletes, exacerbated by unsubstantiated commercial health claims has led to some professional athletes touting gluten-free to be the secret to their success. Forty-one percent of athletes report adhering to a gluten-free diet (GFD), which is four-fold higher than population-based clinical requirements. Many noncoeliac athletes believe gluten-avoidance results in gastrointestinal wellbeing, reduced inflammation and provides an ergogenic edge, despite the fact that limited data yet exists to support any of these benefits. There are several plausible associations between endurance-based exercise and gastrointestinal permeability whereby a GFD may be beneficial. However, the implications of confounding factors, including the risks of unnecessary dietary restriction, financial burden, food availability, psychosocial implications, alterations in short-chain carbohydrates (FODMAPs) and other wheat constituents emphasize the need for further evaluation.

Summary Statement: The recent prevalence of gluten-free athletes has illustrated the multifaceted and potentially detrimental or beneficial effects of a gluten-free diet on performance.

7.3 Introduction

The concept of performance extends beyond the actual physical wins or losses in sport. It also encompasses aspects of individual wellbeing performance that are influenced by dietary intakes and beliefs that ultimately may provide a competitive edge (**Figure 7.1**). Noncoeliac, non-gluten sensitive gluten-free athletes (NCA) have rapidly become a prevalent group adopting a gluten-free diet (GFD) as a means to optimize health and gain a performance edge. Athletes' who follow a GFD, fully or partially, for non-clinical reasons are already four times higher than the 5-10% of the general population requiring gluten-avoidance for clinical reasons (97, 142), which include coeliac disease (CD), wheat allergy and noncoeliac gluten sensitivity (NCGS). The rapid uptake of GFDs with high adherence rates are further exacerbated by illustrious commercial claims equating GFDs with enhanced health, as well as some high profile athletes touting this diet to be the secret to their athletic success (68).

This explosion of gluten-free products and NCA adopting this diet raises the question: Is there anything unique about a GFD that may benefit the athlete in competitive performance and/or performance-related parameters including: gastrointestinal (GI) health, inflammation, dietary healthiness and perceptual wellbeing? It continues to be debatable whether the unique physiological stress of athletic training creates an increased susceptibility (39) to gluten or if rates of NCGS are higher in endurance athletes who already have increased GI issues (131). In this review, we examine GFD research conducted on athletes, as well as clinical and population-based dietary investigations with findings potentially applicable to an athletic population. Although the contemporary nature of this area provides limited NCA-specific evidence, this review further explores theoretical connections associated with gluten and gut injury, inflammation, dietary choices and the belief effect to increase understanding of the gluten-free movement amongst NCA and how these elements require further research, or may ultimately impact health and performance.

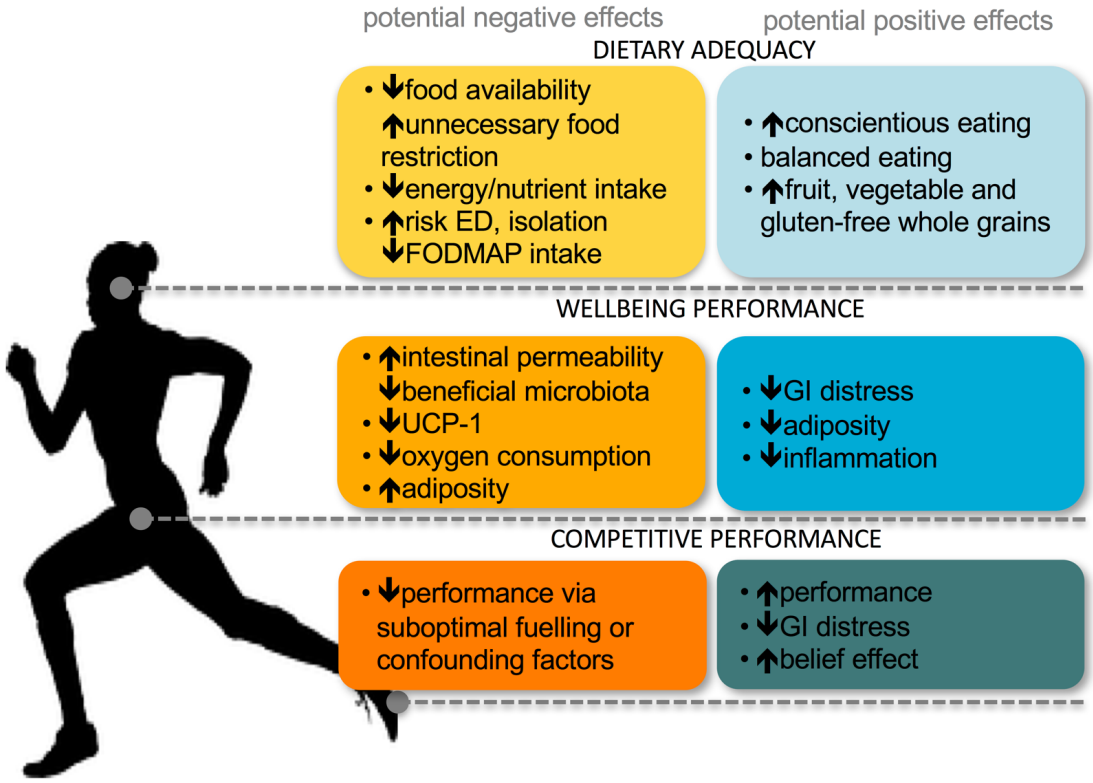

Figure 7.1 – Schematic overview of the potential negative or positive effects/interactions of gluten on athletic performance or health performance. ED=eating disorder, UCP-1=uncoupling protein, GI=gastrointestinal, FODMAP=Fermentable oligosaccharides, disaccharides, monosaccharides and polyols.

7.4 Gluten-related clinical conditions

Gluten is a storage protein composite, with the alcohol-soluble gliadins defined as *prolamins* and the alcohol-insoluble glutenins as *glutelins* (3). Although all grain products, even those considered gluten-free, contain prolamins, only the prolamins found in wheat (gliadin), rye (secalin) and barley (horedin) are the primary peptides associated with immunologic reactions in CD. Gluten is also present in other food products through the addition of grain-based foodstuffs, present as gluten-itself (e.g. soy sauce) or via cross-contamination, such as is common in oats (86). Average intakes of gluten vary (142) geographically and individually. In Western diets gluten intake ranges from 10-20 g.day^{-1} with some individuals consuming up to

50 g gluten.day^{-1} (142). Grain-containing foods and sports foods are a common source of carbohydrate dense nourishment and it is plausible that many athletes ingest above average gluten-containing foods quantities to meet elevated energy and carbohydrate requirements.

Athletes with clinical gluten-related conditions generally experience improvements or complete resolution of a spectrum of intra-intestinal and extra-intestinal symptoms with strict gluten elimination (102). For example, in clinical case reports, athletes presenting with symptoms representative of ill health, including GI issues and poor nutrient status, exhibited improvements in health status, training and competition capacities subsequent to CD diagnosis and the implementation of a GFD (46, 92). However, the vast majority of NCA are self-diagnosing clinical conditions (**Figure 7.2**), NCGS in particular, and subsequently self-prescribing gluten-avoidance. GI symptoms commonly reported in endurance athletes are also believed to be caused by gluten and self-selection of a GFD is readily implemented as a perceived treatment (97). One of the primary reasons for self-diagnosis is likely the arduous double-blind gluten elimination and re-challenge currently employed as the 'best practise' diagnostic tool to determine true NCGS (27), after CD and wheat allergy have been ruled out. Recent research appears to be developing biomarkers (4) to assess NCGS, however, contrary to popular belief no scientifically validated diagnostic biomarker is readily available to confirm NCGS. It is risky for athletes to self-diagnose medical conditions and subsequently adopt a GFD as underlying medical or physiological conditions could be overlooked. Further, non-scholarly advice potentially influencing athletes GFD decisions often lack the individualization required to optimize dietary intake supporting peak athletic performance and may risk injudicious outcomes.

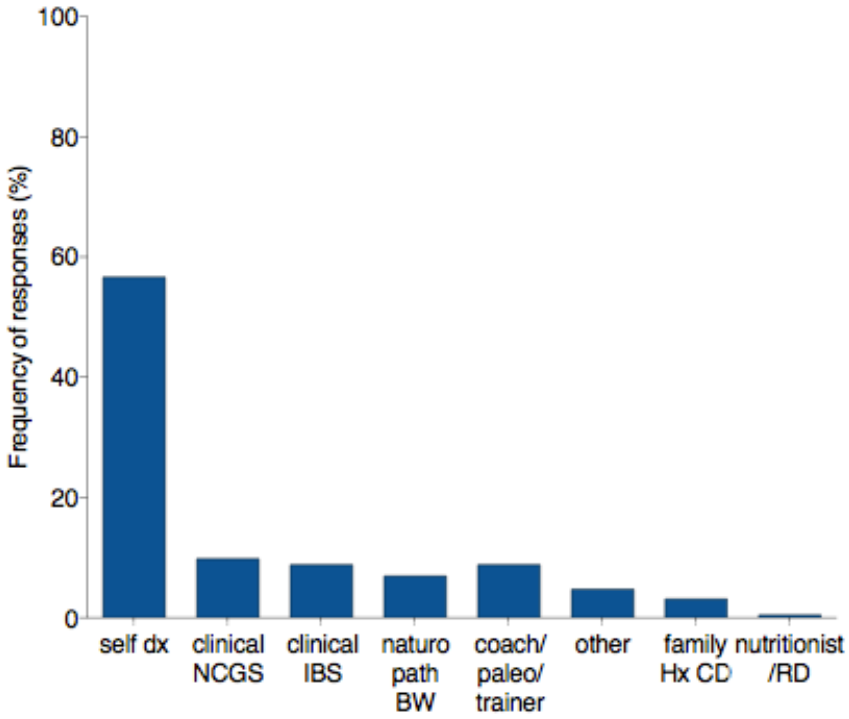

Figure 7.2 – For athletes adhering to a GFD at least 50% of the time the basis for prescription of a GFD. NCGS: non-coeliac gluten sensitivity, IBS: irritable bowel syndrome, BW: bloodwork, dx: diagnosis, hx: history, CD: coeliac disease, RD: registered dietitian.
Modified, by permission, from D. Lis, T. Stellingwerff, C. Shing, K.D.K. Ahuja, and J.W. Fell, 2015, "Exploring the popularity, experiences, and beliefs surrounding gluten-free diets in noncoeliac athletes," *International Journal of Sport Nutrition and Exercise Metabolism*, *25*(1) http://dx.doi.org/10.1123/ijsnem.2013-0247. © Human Kinetics, Inc.

7.5 Gluten-related beliefs on athletic performance

Amongst the 41% of athletes (n=910) that adhere to a GFD over half believe gluten avoidance improves competitive performance (97). Even in athletes not adhering to a GFD approximately a quarter believe gluten avoidance has an ergogenic effect (22, 97). Regardless of the prevalent belief in the performance benefits of a GFD our research group has conducted the only study that has investigated the effects of this diet in NCA on exercise performance (96). This double-blind placebo controlled crossover trial examined the effects of the effects of a 7-day GFD or gluten-containing diet on 15-minute time-trial (TT) performance (97). All food was provided, except for fresh fruit and vegetables, and habitual exercise was replicated between trials, with

16 g.day^{-1} of either gluten or placebo (whey protein) provided in an indistinguishable study food bar. There was no statistical difference between treatments for cycling performance (**Figure 7.3**). Some question remains of whether a longer intervention may account for differential gut flora habituation and thus potentially influence immune parameters or GI symptoms. However, this is not supported by a 4-week GFD in healthy subjects, which demonstrated a reduction in healthy gut bacterial populations (90). Performance is influenced by a plethora of factors and is difficult to accurately measure; however, in our study performance improvement was 100% negligible using magnitude based inference statistics as well as classic statistical approaches (P=0.37). More research is required to definitively elicit whether gluten has any effect on competitive or wellbeing performance. Regardless, this seminal study does not support the popular belief that a short-term GFD has a performance enhancing effect.

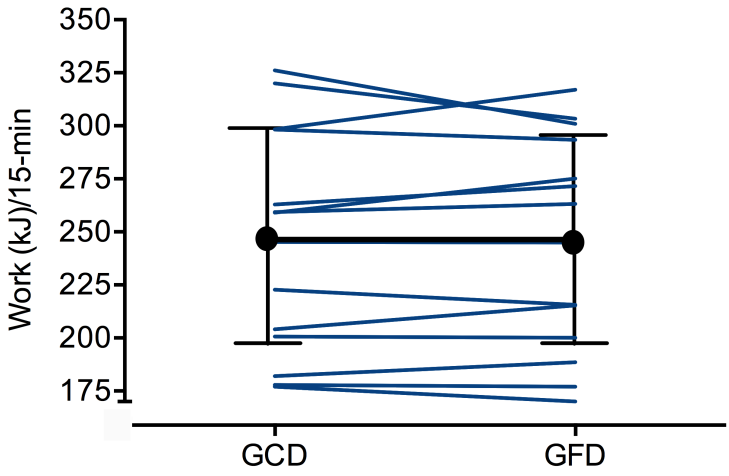

Figure 7.3 – Overall 15-minute time trial performance (kJ) in response to gluten-containing diet (GCD) and gluten-free diet (GFD). — individual performance ● means (SD), n=13. Reprinted with permission, from Lis D, Stellingwerff T, Kitic CM, Ahuja KD, Fell J. No effects of short-term gluten-free diet on performance in noncoeliac athletes. *Med Sci Sports Exerc.* 2015; 47:2563-70. http://www.ncbi.nlm.nih.gov/pubmed/25970665. Medicine & Science in Sports & Exercise.

Although, no direct performance effect has been shown with a GFD when athletes are blinded

to the intervention, in reality athletes are not blinded to dietary changes. Psychological influences and the 'belief' in the effects of a GFD on performance and related parameters, such as pain, have the potential to influence outcomes (10). Beedie et al. (10) and Halson & Martin (66) have discussed the "belief effect" in sport showing a 1-3% improvement in performance. A dietary placebo effect may result in a positive (placebo) effect on performance, experienced both objectively (e.g. improved performance) and/or subjectively (e.g. reduced pain or exertion) (10, 66). Although, no research yet supports any benefits of a GFD for NCA, in actuality the belief in the ergogenic benefits of a GFD may positively influence performance in the field. It is also noteworthy to deliberate situationally appropriate circumstances where a GFD can be used to "tap into" an athlete's belief in a dietary intervention to their advantage (10, 157). However, one needs to appreciate that the complications potentially accompanying a GFD for NCA could be unfavourable to health and performance due to issues in dietary adequacy and other complications, as outlined below.

7.6 Gluten and wellbeing performance

Athletes place their bodies under unique and repetitive stress. Perhaps there are unique aspects to the physical stress of elite training and competition that does provide an underpinning mechanism, which may cause athletes to be more clinically susceptible to gluten.

7.6.1 Exercise gastrointestinal distress

GI distress is reported to occur in 30-50% of endurance athletes (39) and numerous elements can initiate or intensify GI symptoms in an individualized manner during primarily endurance exercise including: mechanical (splanchnic hypoperfusion), physiological (dehydration), psychological (stress) and climatic (heat; 11). Dietary factors such as fibre quantity, carbohydrate type and load (32, 38, 131) and wheat constituents in sensitive individuals may also contribute to GI symptoms (25). Hypothetically, and similarly to NCGS and CD (171),

injury to the intestinal barrier endured by athletes could also create a GI environment more sensitive to gluten, or similar multi-systemic GI side effects of clinical gluten conditions.

Although the gut is partially trainable and splanchnic blood flow is increased with cumulative training (55), elite endurance athletes commonly undergo multiple training sessions per day, which is far less than the 4-5 days required for epithelial cell repair. Investigative research suggests a possible role of increased intestinal permeability leading to excessive absorption of gluten-derived peptides in NCGS (25) which could further potentiate immune related responses. Dehydration and heat further compromise intestinal integrity and athletes training or competing in these conditions may experience exacerbated GI injury (167). Altered digestion of short-chain carbohydrates may also augment GI symptoms triggered during exercise. Reductions in GI symptoms are the most popular rationale for eliminating gluten (97) although our study described above did not show any effect of gluten on GI symptoms (96).

7.7 Immune health

Illness can have a negative impact on health and performance. For athletes that engage in prolonged, strenuous exercise a "J-shaped curve" model has been used to show the relationship between excessive exercise and increased illness rates (119). Numerous dietary strategies are recommended to maintain a robust immune system in athletes (57) but to date a GFD is not one of them for NCA. Many NCA believe gluten elicits undesirable inflammatory responses (97) and in combination with excessive exercise could have an additive toll on the immune system. Our controlled intervention study, discussed above, does not support this conviction. Inflammatory markers (interleukin (IL)-1β, IL-6, IL-8, IL-10, IL-15, tumor necrosis factor (TNF)-α) assessed in response to exercise (pre-, during and post-TT) on the last day of each intervention period showed no significant difference between the gluten-containing diet or GFD (96). Similarly, in IBS patients with belief that gluten triggered symptoms no difference

in c-reactive protein was found after a high gluten, low gluten or a control diet for 1-week in a crossover design (16).

In contrast to short-term human studies rodent-based research in noncoeliac C57B/6 male mice has shown increased IL-6 expression and a trend towards higher TNF levels with an 8-week gluten-containing diet compare to a GFD, suggesting a proinflammatory profile (48). Aside from the obvious disparities in rodent versus human metabolism and disassociation to exercise, the dissimilar observations between studies could be owing to a longer intervention length in the rodent study, unconnected to exercise and cytokines measurements taken from adipose tissue. Nonetheless, gluten or wheat constituents are central to the inflammatory response in sensitive individuals (171) and this can be associated to the above-mentioned exercise-induced intestinal permeability (38, 167). Therefore, the substantial and repeated stress placed on an athletes' immune status and the subsequent effects on the inflammatory state, highlights the need for a greater understanding on the effects of gluten or wheat constituents as a component of immunonutrition strategies.

7.8 Body composition

Athletes eliminate gluten to promote weight loss or improve body composition for sport (97) although evidence to support this is lacking (50). Most research has analysed weight changes pre- and post GFD adherence in CD (161) but the dietary control is inconsistent and the complexity of confounding factors (e.g. type 1 diabetes, chronic inflammation) limit its applicability to NCA. Surprisingly, in CD populations there is an increased risk of obesity with GFD adherence suggested to be linked to increased nutrient absorption and intakes of high fat/sugar gluten-free products (161). While there are no studies in noncoeliac humans investigating the effect of gluten on body composition, studies in male C57B/6 mice suggest that a gluten-containing diet compared to an isocaloric GFD increases fat deposits, regardless of whether the diet is high fat or of normal fat content (48, 151). The increased body weight

and adipose tissue in gluten-fed mice was also associated with impaired glucose homeostasis, a decrease in fasting and non-fasted oxygen uptake and lowered energy expenditure and increased adipocyte content of proinflammatory cytokines (48). This data has limited transferability to NCA as the macronutrient breakdown of the diets were not representative of typical athlete diet recommendations (162). In general, athletes aim to optimize power to weight ratio by achieving low body fat levels and if a gluten-containing diet promoted adiposity it would obviously be counterproductive.

7.9 Gluten and nutritional adequacy

Our recent questionnaire based publication showed that the majority of NCA adopting a GFD (at least 50% of the time) are recreationally competitive endurance athletes (~70% of 910 respondents) with the conviction that it is healthier, improves conscientiousness of food choices and promotes overall more balanced eating (97). It is debatable whether a GFD equates to dietary changes resulting in a healthier or less healthy diet, or if other dietary habits are subsequently modified resulting in improved or worsened eating behaviours. Hype about this diet brings in the question of dietary and nutritional adequacy and the issue of suboptimal fuelling risk as described in other elimination-type diets (156).

NCA adhering to a GFD do so in varying degrees; ranging from periodic gluten elimination, elimination 1-2 weeks before competition or up to 100% of the time (97). Although adherence rates vary, enhanced dietary mindfulness is suggested as an outcome to avoidance of gluten-containing products (51, 97). Converting to a GFD plausibly results in some athletes increasing their conscientiousness of healthy balanced eating, increasing fruit and vegetable and whole grain intake and decreasing processed food selections (51); food choices all underpinning good sport nutrition practises. The variable nature of dietary choice highlights the fact that individual food selection may be an instrumental predictor of the overall healthfulness and nutritional adequacy of a GFD for NCA (147). However, the proliferation of the gluten-free food products

market results in both an increase of unhealthy gluten-free products as well as the production of more nutrient-rich pseudo-cereals, such as amaranth, buckwheat and quinoa, replacing corn and rice flour (127). These substitutions could potentially reduce the risk of omitted dietary sources of B-vitamins and iron that are critical for metabolism and athletic adaptations.

An athletes' dietary intake is unique in that it must be optimized to maintain sufficient energy intake and to augment training adaptation and health. Nutrition interventions may purposefully integrate periodised energy deficits to augment sport-specific body composition. However, elimination diets have been linked to non-strategic suboptimal energy intakes and could potentiate low energy availability and associated risks, especially in endurance athletes (156). Analysis of the capacity of a GFD to support athletic energy demands has not been conducted so it is unknown if the dietary restriction associated with this diet compromises energy availability. Clinical investigation in this area is dated and fails to account for newer gluten-free food alternatives now accessible. The only recent study investigating energy intakes in GFD compared the nutritional status of patients with CD adhering to a strict long-term (2-year) GFD to healthy controls and found energy intake to be similar in both groups (6). However, the multifactorial nature of fuelling athletes also encompasses unique and complex eating behaviours that may overlap with avoidance of gluten-containing grains. Some behaviours may include restriction of grain-based foods completely, consumption of a limited low energy density diet or with orthorexia nervosa behaviours under the blanket of a GFD, particularly in weight dependant sports (114). Additive factors such as limited accessibility to gluten-free foods when travelling or competing abroad further complicate the ability of a GFD to reliably support athlete energy requirements (67).

Macronutrient and some micronutrient requirements for athletes are often higher compared to the general population (162). Historically, a GFD has been associated with suboptimal intake

of protein, fibre, B-vitamins and iron alongside increased fat and sugar intake (161). For athletes there is the additional concern of insufficient carbohydrate associated with the exclusion of gluten-containing foods (97). Contemporary studies, conducted in different countries with varying methodologies, have presented conflicting evidence concerning the macronutrient and micronutrient adequacy of gluten-free foods for the general population (161). Three studies have profiled the nutritional quality of 63 to 3213 gluten-free food products (e.g. staple items: pasta, breads, ready-to-eat breakfast cereals) compared to gluten-containing equivalents and also compared the Health Star Rating (an algorithm based on energy, total sugar, sodium, saturated fat, fibre and protein) (175) or macro- and micronutrient composition (85, 112). For athletes choosing gluten-free products, there is no obvious nutrient shortfall in most of these products compared to gluten-containing equivalents, but no health benefit either.

Quantification of the healthfulness of gluten-free foods is important to discuss as there exists a belief among athletes that eating gluten-free equates to healthier food choices (97). Aside from being an effective treatment for the spectrum of gluten-related disorders evidence-based research supporting a GFD as a "healthier" option for NCA is lacking (50). Several studies have analysed a GFD for nutritional appropriateness compared to a gluten-containing diet using diverse methodologies in CD populations. Approaches used include prospective dietary analysis (140), virtual comparative analysis (111) and GFD compared against controls (6). Some statistical differences were found with lower protein or lower fibre but there were no consistent findings across all studies that clearly indicate a difference in this non-athletic population. The slightly lower protein content indicated across gluten-free products and a GFD is negligible and of little practical significant as athletes are recommended to rely upon meat/alternatives and dairy as sources of protein, not grains (162). Overall, these studies indicate that the distribution of macronutrients was similar between a GFD and gluten-

containing diet (6, 111, 140), however there have been no studies published examining nutritional adequacy of GFDs in varying elite athlete populations. Due to the scarce evidence in this area and inherent error associated with diet record collection it is not possible to conclude whether a GFD provides an optimal macro- or micronutrient profile for athletes, thus GFD adequacy should be assessed individually.

Some athletes are so focused on eating gluten-free that they overlook the importance of eating a balanced diet to support training and recovery. Complications possibly arising from unnecessary food restriction may include; increased anxiety around food (orthorexia nervosa), time commitment, expense, social concerns and interference with appropriate medical intervention (51, 149). An enormous amount of time and money is spent by individuals with CD on label and food checking, at an estimated 10-20 hours per month (132), plus an estimated 206-267% increase in food expenses (51, 112). Social consequences also present, such as difficulty eating outside of the home, with friends, family or team (51) or in various training/competition locations where gluten-free foods may be less available or inaccessible may compromise optimal fuelling. For some athletes, the lifestyle complications and challenges in supporting optimal fuelling or nutrient intake on a GFD may be an unnecessary burden if a GFD is not a clinical necessity. See et al. (86) summarize they key dietary planning strategies which may reduce the nutritional risks historically associated with a GFD, however athletes' unique nutritional requirements may be elevated and capability of a GFD to reliably meet these has not been evaluated. It is therefore prudent to acknowledge that dietary restriction, or an elimination diet, may pose a risk for optimal fuelling for sport performance, particularly for athletes already under fuelling.

7.10 Are FODMAPs a major gluten symptom confounder?

Gluten-free markets are predicted to experience continued growth, but emerging market reports also predict low FODMAP diets to eventually become the 'new' gluten-free (106). FODMAPs are a family of short-chain carbohydrates (including fructans), are found naturally in foods, and are particularly prevalent in wheat, some fruits/vegetables and legumes (9), and thus appropriately named as Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols. Coincidently a GFD also reduces fructan and galactooligosaccharides intake and some researchers suggest that the change in dietary fructan load, rather than gluten itself, is the primary GI symptom modulator (52, 115). For some individuals, fructans and other FODMAPs are poorly absorbed in the small intestine where they increase luminal fluid content and possibly affect gastric motility (152). Poorly absorbed, they subsequently transit to the colon as products for fermentation by colonic bacteria, resulting in GI symptoms such as diarrhoea and flatulence (152). Although no data is yet published in athletes without IBS, it is conceivable that residual FODMAPs in the small intestine (ileum) and colon or intake of FODMAPs during training potentiate GI distress during and after strenuous exercise.

A low FODMAP diet is a strategy efficaciously applied in the treatment of IBS (152), but also practiced by some athletes to decrease GI symptoms (41). Investigation of the role of FODMAPs in athletes with persistent excise-induced GI symptoms is in its infancy. However, preliminary work has been conducted by our group quantifying high FODMAP food/category elimination in athletes (95). Self-reported data indicates that 51% of athletes (n=465 of 910) eliminate at least one high FODMAP food or food category with the aim to reduce GI symptoms. After elimination, reported symptom improvement ranged from 68.2% (polyols) to 83.7% (lactose) (95). In this study athletes self-selected FODMAP categories that were queried alongside a short list of high FODMAP food examples (e.g. fructose: apples, mango, honey) and they may have been familiar with FODMAPs and/or only the high FODMAP foods listed.

Lactose (86.8%, n=402 of 465) was the most frequently eliminated followed by galactooligosaccharides, fructose, fructans and polyols to a much lesser extent. Lactose elimination was also the most frequently reported to occur alongside gluten avoidance which parallels population-based and clinical findings (95, 176). From an intervention perspective, one case-study report of a multi-sport athlete with persistent running-specific exercise-induced GI symptoms reported measurable symptom improvement with a 3-day low FODMAP diet prior to and throughout 3-days of strenuous running training (94). Though there are limitations associated with self-report data these initial findings from our group suggest that perceived gluten-triggered GI symptoms in athletes might be due to FODMAPs, particularly fructans and lactose as potential symptom modulators, although more placebo-controlled double-blind studies are required to confirm this.

7.11 Conclusion

Widespread media validation continues to drive the popularity of GFDs forward, yet this diet has not been shown to affect, either positive or negatively, competitive performance or symptoms of GI health and inflammation and/or nutritional status in NCA. Sport nutrition practitioners are faced with a unique challenge when advising on the appropriateness of GFDs for NCA, as most NCA self-prescribe this diet based on non-peer reviewed evidence. Theoretically mechanisms unique to athletes may increase susceptibility to gluten locally and systemically with exercise-induced GI injury, but these have not been directly explored. Direct confounding factors of concern with gluten-avoidance in athletes include caloric fuelling challenges, unnecessary restrictive eating practises or the risk of overlooking appropriate medical diagnosis. While this "belief effect" may be responsible for NCA perceived benefits of going gluten-free, practitioners determining the appropriateness of a GFD for a NCA should first consider possible underlying GI disorders or other food intolerance, as well as potential risks associated with unnecessary food restrictions and cost. Current limited evidence does not

support the performance or health benefits of a GFD for NCA. Adoption of this diet should be carefully deliberated and prescribed under appropriate medical and/or dietetic guidance.

Chapter 8: Thesis summary, future directions and conclusions

8.1 Thesis Summary

The most important findings arising from the studies undertaken in this thesis are established upon both observational and intervention studies. Observational investigations quantified the GFD movement amongst athletes worldwide, concluding that fourfold more athletes follow this dietary regime than estimated to be clinically required. GI symptoms were confirmed as a predominant rationale for NCA going gluten free alongside the belief that a GFD reduced inflammation and provided an ergogenic edge. Elimination of foods high in FODMAPs was also confirmed to be a prevalent dietary strategy utilized by NCA aimed at reducing GI distress. Although widespread belief exists in the beneficial effects of these diets, particularly GFDs, the findings from this thesis work were the first to disseminate qualitative and quantitative conclusions about dietary practises, experiences, beliefs and sources of information regarding GFDs and high FODMAP foods amongst NCA (95, 97).

Further seminal work was conducted to investigate the effects of a short-term GFD in NCA on performance and related parameters including: systemic inflammation, intestinal injury and perceptual wellbeing (96). Under well-controlled diet and exercise conditions a GFD demonstrated neither a beneficial nor a negative effect on performance. Measures of GI health, inflammation and perceptual wellbeing were also similar during the GCD compared to GFD periods in NCA (96). In the succeeding preliminary investigations, FODMAP restriction did show emerging promising results (e.g. GI symptom reduction). Measurable GI symptom reduction was observed in a multisport athlete with persistent exercised-associated GI symptoms while following a short-term low FODMAP intervention diet compared to his habitual high FODMAP diet (94). Similarly, a low FODMAP diet demonstrated a reduction in

daily GI symptoms compared to a high FODMAP diet in clinically healthy runners with persistent exercise-associated GI distress.

A GFD and avoidance of high FODMAP foods are prevalent and emerging dietary strategies adopted by athletes predominantly to reduce GI symptoms. Athletes often self-implement perceived beneficial dietary strategies that lack supportive evidence. A belief effect may underpin the perceived benefits or the intervention may actually have an impact which has yet to be scientifically validated. Also, going gluten-free may consequently reduce the intake of certain FODMAPs, or vice versa, low FODMAP can result in reduced in gluten intake. The research conducted within this thesis is the first to bridge practical behaviours relating to GFD and FODMAPS and quantify the effects of these dietary regimes on GI symptoms and performance in athletes. Findings from this thesis have rapidly become an influential evidence-base for sport nutrition practitioners advising on the effects of GFD for NCA (5). Further, these results have provided novel insight regarding the use of FODMAP manipulation, rather than gluten, to address GI issues in symptomatic athletes. Overall, the work conducted in this thesis suggests that a GFD does not have a beneficial or negative effect on performance, GI health, inflammation or overall wellbeing. Instead, FODMAP manipulation may be an effective and innovative addition to the sport nutrition practitioner's toolbox for management of exercise-associated GI distress. Practitioner supported, systematic and individualized approaches will be required for the successful, and potentially efficacious implementation of this dietary approach.

8.2 Limitations

8.2.1 Dietary intervention length

The applicability of lengthier dietary intervention periods depends on the primary research question and the logistical methodologies for prolonged dietary control, which become exponentially more difficult during long-term interventions. In many ways, a shorter intervention, as modelled in the studies within this thesis (Chapter 3, 5, 6), are ideal for investigating GI distress due to the rapid turnover of GI tract proteins. Animal based and unpublished human data (152, 170) has demonstrated that protein turnover in the GI tract is five times higher than muscle protein synthesis; essentially yielding a new GI tract in 5 to 7 days. However, it can be argued that longer interventions would allow time more time for physiological changes to manifest, such as changes in the microbiome, and may better capture effects of dietary interventions on GI measures.

Another element to consider in both short and long term interventions is energy balance. Negative energy balance, common in endurance athletes (160), can decrease the rate of protein synthesis (122). In both long and short-term interventions reduced epithelial protein synthesis is likely to impair gut barrier function and increase permeability. This may be a reason low energy availability has been associated with frequent GI symptoms (160). Coupled with exercise stress and dietary triggers, negative energy balance could be a perfect storm for amplified GI issues. However, currently, no one has examined the effects of gut function or inflammation in various states of energy availability. Although the work conducted within this thesis only briefly discussed the effects of energy balance on GI symptoms this is likely a confounding element of acute and chronic GI health in athletes and requires further investigation.

Adverse symptoms triggered by gluten and/or FODMAPs are reported to improve in a few hours to days after dietary elimination (47, 123); however, study methodology with a longer duration of dietary adherence would be valuable to account for differential gut flora habituation as changes in the microbiota influence GI and immune health, performance and related parameters (64, 90, 154). It is important to note that the effects of dietary manipulation on various outcomes of athletic performance may be difficult to monitor as training adaptations that can also occur over a longer intervention period (weeks to months) would likely confound dietary-influenced performance changes. In addition, any negative dietary influences on microbiota composition and population may be countered by the promotion of gut micro-organism diversity by exercise and observation of any negative outcomes may require longer interventions (29). In healthy controls a reduction in bacterial abundance and favourable bacterial populations have been shown in a low FODMAP compared to a higher habitual FODMAP diet as well as a GFD compared to a habitual GCD, demonstrated after 3-4 weeks of adherence (40, 62, 90). While it would be ideal to implement lengthier interventions, these are more intrusive for the athlete and would challenge dietary adherence and the ability to control and replicate training and food intake. Nonetheless, future investigations are encouraged to incorporate longer dietary interventions and possibly longer washout periods, provided the methodology enabled adequate control and adherence.

8.2.2. Prescribed exercise

Intestinal injury and GI symptoms are largely influenced by physiological and mechanistic factors which are further increased with longer, more strenuous exercise and specific modalities, such as running (38). IFABP measures taken before, during and after the cycling performance trial in the GFD study (Chapter 3) indicate that exercise stress was adequate to induce acute epithelial injury and thus intestinal permeability (100, 169). In the prescribed running bouts (Chapter 5, 6) intestinal permeability was not measured, so it is unknown if the

mechanical and physiological stress of these sessions were robust enough to cause epithelial injury, which would expectedly augment GI symptoms. Increased permeability is sometimes associated with GI symptoms (125); however, a measurable difference in GI symptoms during exercise was not observed with either the gluten or low FODMAP interventions (Chapter 3, 5, 6). To gauge changes in GI symptoms between diets, more stress placed on the gut may have been required to measure possible dietary impacts. Forthcoming investigations should consider exercise performance protocols that are longer and/or multi-day or under heat stress, more strenuous, with the mechanical load of running and the requirement of during-exercise fuelling. For example, perhaps a marathon race simulation is required to detect greater changes in GI symptoms between groups, particularly during exercise. Additionally, it would be practical to assess the effects of gluten-containing versus gluten-free and low FODMAP vs high FODMAP sport food ingestion during exercise sessions that warrant carbohydrate ingestion (75).

8.3. Future studies arising from thesis results

8.3.1. Analysis of nutrition quality of a GFD and low FODMAP diets in free-living athletes

Wide-ranging beliefs exist surrounding the nutrition adequacy of a GFD or the subsequent dietary changes that may occur. Several investigations, with varied methodology, have attempted to quantify the nutritional adequacy of a GFD in clinical and healthy control populations (111, 134). Based on the review of the literature there is no conclusive evidence that energy, macro- or micronutrient intakes are significantly different with a GFD compared to a GCD. However, athletes may have elevated energy and nutrient needs compared to the general population. Dietary restriction may risk suboptimal dietary intake, compromise ideal fuelling for athletic demands, amplify risk of developing orthorexia nervosa and make it more challenging to fuel abroad. Although our findings did not support any benefit of a GFD for NCA, future research should investigate the adequacy of a GFD in free-living NCA athletes,

self-selecting food, and further quantify likely environmental and psychosocial challenges as well as character traits of gluten-free athletes (15, 86, 149).

Low FODMAP diets have been shown to be nutritionally adequate in clinical and healthy populations (64, 123); however, advanced dietary support and planning has been applied in these studies. The nutritional adequacy of self-selected low FODMAP diets has not been investigated alongside the elevated and unique nutritional requirements characteristic of athletes (162). Dietary restriction has the potential to compromise optimal nutritional intake as well as trigger related psychosomatic stress. In free-living athletes, future studies should consider evaluation of self-selected short- and long-term low FODMAP diets for potential influences on nutritional intake as well as overall wellbeing.

8.3.2. Preceding gluten-free dietary beliefs

Inclusion criteria for the dietary intervention studies required participants to not be on any special diet 6-weeks prior to the intervention. It is likely that participants had a range of beliefs regarding the effects of a GFD on health and performance which was representative of our questionnaire-based findings (97). Although recruitment and ethical approval may prove challenging, future studies should consider inclusion criteria that requires participants to believe they have NCGS but are agreeable to eat gluten in a blinded manner. It would be further interesting to assess the probable belief effect (10, 66) associated with gluten and use a deception technique to evaluate the effects of informing participants they were eating a GFD when they were in fact being fed hidden gluten.

8.3.3. Parallel design GFD and FODMAPs

There is great potential to design a parallel group design to assess the effects of gluten and FODMAPs on performance, GI health and a myriad of parameters influencing performance.

Logistics and elevated sample sizes would prove challenging; however, a crossover design in this manner could include the following four diet clusters:

1. gluten-free with high FODMAPs
2. gluten-free with low FODMAP
3. gluten-containing with high FODMAPs
4. gluten- containing with low FODMAP

This study design could potentially delineate if gluten, FODMAPs or both were major triggers for GI symptoms in NCA.

8.3.4. FODMAP reintroduction

In clinical practise, adherence to a complete long-term low FODMAP diet is not advised (54). In a systematic manner practitioners aim to determine the specific FODMAPs eliciting GI symptoms and individually reintroduce tolerable amounts of other high FODMAP foods (7). Relatedly, carbohydrate absorptive capacity of the intestine is adaptable and modified by the carbohydrate content of the diet (75, 79). Increases in intestinal carbohydrate transporters are shown with higher dietary carbohydrate intakes, thus improving the ability to ingest, oxidize and tolerate more carbohydrate (125). Improved ability to tolerate and oxidize greater amounts of carbohydrates is favourable for athletes engaging in sports with high carbohydrate demands for fuel (32). It is interesting to consider that, in some athletes with FODMAP sensitivity, a period of strategic reintroduction may increase the amount or type of FODMAPs tolerated without detrimental symptoms. Expanding practical athlete-specific FODMAP approaches are essential in applying this diet external of the clinical setting. Future studies should investigate the reintroduction of FODMAPs and the potential to increase tolerance to specific FODMAP triggers.

8.4. Concluding comments pertaining to practical application

Novel evidence from the research conducted throughout this thesis will expand the sport nutrition practitioner's strategies to treat exercise-associated GI symptoms. Although, our GFD intervention study did not support the beneficial effects of a GFD on GI symptoms or the parameters assessed, practise-based nuances should be considered when assessing the appropriateness of a GFD in the field when working with athletes. A low FODMAP diet did demonstrate promising beneficial effects on GI symptoms in some athletes potentially supporting its efficacy. FODMAP reduction may be a strategy auxiliary the sport nutrition practitioners' toolbox for the treatment of GI distress in scenarios where a gluten-free or low FODMAP approach may be appropriate.

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Appendices

Appendix 1 – Poster Sport Dietitians of Australia Conference 2014

Exploring the popularity, experiences and beliefs surrounding gluten-free diets ir non-coeliac athletes

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INTRODUCTION

Adherence to a gluten-free diet (GFD) for non-coeliac athletes has become increasingly popular despite a lack of either supportive medical or ergogenic evidence.

AIM

This study aimed to quantify the demographics of non-coeliac athletes (NCA) and determine related experiences, perceptions and sources of information related to a GFD.

METHODS

Subjects: Athletes, non-coeliac, (n=910, female=528, male=377, no gender selected=5) recruited globally.

Overview: A 17-question electronic survey using SurveyMonkey collected data about athletes and GFDs:

(1) Demographics (age, gender, sport, level of competition)
(2) GFD adherence, if any
(3) Rate of gastrointestinal (GI) symptom occurrence and additional symptoms
(4) Perceptions pertaining about GFDs and athletic
(5) Sources of GFD information

Survey development: Survey was developed/refined following feedback from registered dietitians working across the National and Olympic level.

Data Management: Some responses were re-categorised or combined prior to data analysis. Survey design was targeted to identify GFD adherence in three sub-categories (adherence to a GFD 50-75%, 75-89% and 90-100% of the time). Responses were analogous to support grouping athletes into two groups:

1. **GFD>50**: athletes that adhered to a GFD over 50% of the time.
2. **GFD<50**: athletes that adhered to a GFD less than 50% of the time.

Statistical Analysis: Excel (version 14.3.7, USA) to download and collate survey data. GraphPad Prism (version 6.02, USA) for graphic representation. Stata (STATA version SE12, USA) to compare the responses between the GFD>50 and GFD<50 groups with logistical regression.

RESULTS

Table 1. Demographic characteristics of athletes

	GFD<50 (n=535)	GFD>50 (n=375)
Age	n (%)	n (%)
18-24 years	169 (31.6%)	95 (25.3%)
25-30 years	127 (23.8%)	98 (26.1%)
31-40 years*	126 (23.6%)	109 (29.1%)
41-50 years	64 (12.0%)	48 (12.8%)
>50 years	29 (5.4%)	20 (5.3%)
Sport category	n (%)	n (%)
Endurance*	335 (62.6%)	262 (69.9%)
Power	40 (7.5%)	26 (6.9%)
Skill	10 (1.9%)	11 (2.9%)
Swim/rowing	38 (7.1%)	19 (5.1%)
Intermittent	77 (14.4%)	28 (7.5%)
Weight classified, aesthetic	19 (3.6%)	7 (1.9%)
Winter	9 (1.7%)	9 (2.4%)
Fitness	7 (1.3%)	13 (3.5%)
Level of competition	n (%)	n (%)
Recreational*	116 (21.7%)	121 (32.3%)
Recreational competitive	122 (22.8%)	9 (2.4%)
Provincial/state	62 (11.6%)	26 (6.9%)
National	104 (19.4%)	60 (16.0%)
International	57 (10.7%)	33 (8.8%)
World/Olympic qualifier	35 (6.5%)	21 (5.6%)
World/Olympic medallist	29 (5.4%)	18 (4.8%)
Professional	10 (1.9%)	5 (1.3%)

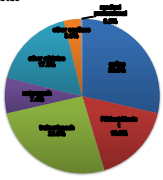


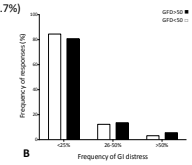
Figure 1. Sources of GFD information
Online, trainer/coach and other athletes were the most accessed sources GFD information.

RESULT CONTINUED

GFD Adherence
41% of athletes followed a 50-100% of the time (GFD>50).
GFD>50 group:
- GFD 90-100% of the time (50.0%)
- GFD 75-89% of the time (7.5%)
- GFD 50-74% of the time (42.0%)

58.8% of athletes followed a GFD less than 50% of the time (GFD<50).
GFD<50 group:
- Purchased gluten-free products once in a while (10.7%)
- GFD sporadically (few days/month) (9.3%)
- GFD 1-2 weeks before competition (0.7%)
- Did not eat GFD (38.8%)

Figure 2. GI distress
More frequent GI distress, 26%-50% and over 50% of the time were reported in the GFD>50 compared to the GFD<50 group.



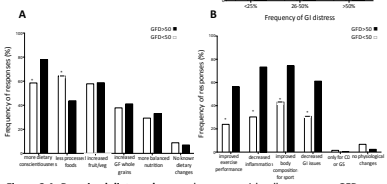


Figure 3 A. Perceived dietary changes that occur with adherence to a GFD.
B. Perceived physiological changes GFD>50 and GFD<50 that occur with adherence to a GFD. CD: coeliac disease, GS: gluten sensitivity.
*Significantly different between GFD>50 and GFD<50.

Experiences / Symptoms
Gluten removal reportedly resolved symptoms believed to be triggered by gluten in 87.4% of GFD>50. Symptoms categorized: abdominal/gastrointestinal, nutritional, physiological and skin indicators. Abdominal/gastrointestinal symptoms alone (16.7%) and in conjunction with two (30.7%) or three (35.7%) additional symptoms were the most highly reported to be triggered by gluten in GFD>50 athletes.

CONCLUSION

- The 41.2% of NCA athletes following a GFD is greater than the prevalence in the general population estimated to benefit clinically from a GFD (~5-10%) *(Hadjivassiliou et al. 2010, Sapone et al 2012).*
- Prescription of a GFD amongst athletes does not result from evidence-based practice suggesting two possible hypotheses: (1) athletes follow a GFD due to perceived physiological improvements that may coincide simultaneously with other dietary changes; (2) the perception that gluten elimination will provide health benefits and an ergogenic edge in NCA.

References
Sapone, A., Bai, J. C., Ciacci, C., Dolinsek, J., Green, P. H., Hadjivassiliou, M., Fasano, A. (2012). Spectrum of gluten-related disorders: consensus on new nomenclature and classification. *BMC Med, 10*, 13.

Hadjivassiliou, M., Sanders, D. S., Grunewald, R. A., Woodroofe, N., Boscolo, S., & Aeschlimann, D. (2010). Gluten sensitivity: from gut to brain. *Lancet Neurol, 9*(3), 318-330.

Appendix 2 – Poster American College of Sports Medicine Conference 2015

No effects of a short-term gluten-free diet on performance in non-celiac athletes

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INTRODUCTION: Adherence to a gluten-free diet (GFD) for non-celiac athletes has become increasingly popular despite a paucity of supportive clinical or ergogenic evidence. Our recent study indicated that 41% of non-celiac athletes followed a GFD, while only 5-10% of the general population medically necessitates gluten-avoidance.

PURPOSE: To investigate the effects of dietary gluten on exercise performance, gastrointestinal (GI) symptoms, well-being and intestinal injury, in non-celiac endurance athletes.

METHODS: Thirteen competitive endurance cyclists (8 males) with no positive clinical screening for celiac disease or history of irritable bowel syndrome (mean±SD; age: 32±7 years; weight: 71.1±13.4kg; height 177.0±11.8cm, VO_{2max} 59.1±8.0ml.kg^{-1}.min^{-1}) were allocated to a seven day gluten-containing diet (GCD) or GFD separated by a 10-day washout in a double-blind, randomized controlled study. Cyclists ate a GFD alongside either gluten-containing or gluten-free food bars (16g wheat gluten per day) while habitual training and nutrition behaviors were controlled. During each diet, cyclists completed the Daily Analysis of Life Demand for Athletes (DALDA) and GI questionnaires (post-exercise and daily). On day seven cyclists completed a submaximal steady-state (SS) 45-min ride at 70% peak power and followed by a 15 minute time-trial (TT). Blood samples were taken pre-exercise, post SS and post TT to determine intestinal fatty acid binding protein (IFABP). Mixed effect logistic regression was used to analyze data. **RESULTS:** TT performance was not significantly different (p=0.37) between the GCD (244±53kJ) and GFD (245±55kJ). GI symptoms during exercise, daily, and DALDA responses were similar for each diet (p>0.11). There were no significant differences in IFABP (p=0.69) responses.

CONCLUSIONS: A short-term GFD had no overall effect on performance, GI symptoms, well-being, intestinal injury in non-celiac endurance athletes.

INTRODUCTION

- Previously, our data showed that over 40% of non-celiac athletes follow gluten-free diet (**GFD**) at least half of the time[1].
- Many athletes (30%) self-diagnose gluten-related conditions and self-prescribe a GFD[1].
- Athletes believe that a GFD improves performance, gastrointestinal (GI) health, psychological well-being and decreases inflammation.

AIM

To determine the effects of a GFD in non-celiac athletes on:

① Exercise performance
② Intestinal Injury
③ GI symptoms
④ Perceived well-being
⑤ Marker of systemic inflammation.

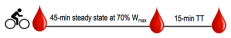
METHODS

Athletes: Competitive non-celiac cyclists (n=13, female=5, male=8) (mean±SD; age: 32±7 years; weight: 71.1±13.4kg; height 177.0±11.8cm, VO_{2max},59.1±8.0ml.kg^{-1}.min^{-1})

Study design:

- Seven-day gluten-containing diet (**GCD**) or GFD (separated by 10-day washout). Habitual training and nutrition behaviors were controlled and replicated between trials.

- Performance test was completed on day-7 of each trial.



METHODS continued

Food Preparation

- 100% of all meals (all gluten-free) were provided.
- Study food bars containing placebo or gluten (16g total, 2 bars/day) were consumed throughout the day to mimic typical Western diet.

Data collected daily

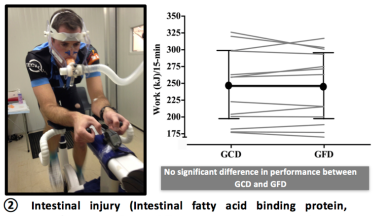
- Daily and post-exercise GI questionnaires
- Daily Analysis of Life Demands for Athletes (DALDA)

Data collected during performance trial (day 7)

- Performance (kJ) 15-min TT
- Acute intestinal injury, intestinal fatty acid binding protein (IFABP)
- Markers of systemic inflammation (cytokine response: IL-1β, IL-6, IL-8, IL-10, IL-15, TNF-α)

RESULTS

① **Exercise Performance** (15-min TT)

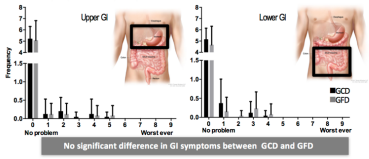


No significant difference in performance between GCD and GFD

② **Intestinal injury (Intestinal fatty acid binding protein, IFABP):** No significant difference in acute intestinal injury (p=0.69).

RESULTS continued

③ **GI symptom questionnaire:** Frequency of GI symptoms during exercise over 7-day period. Values are median (range).



No significant difference in GI symptoms between GCD and GFD

④ **Perceived well-being**: DALDA scores of "worse than normal" between the GCD (26±19) and GFD (27±18) were not different (p=0.26).

⑤ **Markers of systemic inflammation:** No significant difference in inflammatory cytokine responses (p>0.05).

CONCLUSIONS

- A 7-day GFD does not have a beneficial or a negative affect on cycling performance.
- A 7-day GFD does not affect GI health, overall well-being, intestinal injury or systemic inflammation in non-celiac athletes compared to a GCD.
- Based on these findings it is recommended that athletes seek evidence-based advice before adopting a GFD for non-clinical reasons to ensure that nutrition intake supports individualised and optimal fueling for sport performance.

Acknowledgements: Food donation from Orgran, PureBred, Brookfarm. Research funding support from King & Amy O'Malley Trust, Sports Medicine Australia, Sports Dietitians Australia and Canadian Sport Institute Pacific.

References

1. Lis D, Stellingwerff T, Shing CM, Ahuja KD, Fell J. Exploring the Popularity, Experiences and Beliefs Surrounding Gluten-Free Diets in Non-Coeliac Athletes. *Int J Sport Nutr Exerc Metab.* 2014.

Appendix 3 – Poster Canadian Society for Exercise Physiology Conference

From gluten to FODMAPs: Dietary strategies to combat gastrointestinal symptoms in athletes

UNIVERSITY of TASMANIA AUSTRALIA

Dana Lis[1], Kiran Ahuja[1], Cecilia Kitic[1], James Fell[1], Trent Stellingwerff[1,2]

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[2] Canadian Sports Institute Pacific, British Columbia, Canada.

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CANADIAN SPORT INSTITUTE — INSTITUT CANADIEN DU SPORT

Study 1: Questionnaire to assess the popularity and belief-factors of gluten-free diets in athletes

METHODS

NCA (n=910) nonceliac recruited globally completed an electronic survey that collected data about gluten-free diets (GFD) and fermentable oligo-, di-, monosaccharides and polyols (FODMAPs) .

Data collected

1. Demographics (age, gender, sport, level of competition)
2. GFD adherence and FODMAP avoidance
3. Gastrointestinal (GI) and other symptoms
4. Perceptions about GFD and athletic performance

RESULTS

- 41% of NCA adhere to a GFD at least half of the time with 81% reporting GI symptom improvement.
- 55% of nonceliac athletes avoid at least 1 FODMAP food/nutrient with up to 83% reporting GI symptoms improvement.
- Physiological beliefs about GFDs (Fig.1).
- Basis of prescription for adherence to a GFD (Fig 2.)

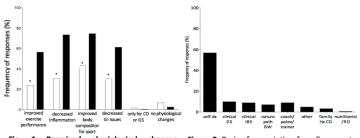

Fig. 1 Perceived physiological changes believed to occur with adherence to a GFD CD: coeliac disease, GS: gluten sensitivity. ■ GFD □ Gluten-containing diet (GCD) *Significantly difference

Figure 2. Basis of prescription for adherence to a GFD. GS: gluten sensitivity, IBS: irritable bowel syndrome, BW: bloodwork, dx: diagnosis, hx: history, CD: coeliac disease, RD: registered dietitian.

CONCLUSIONS

Four fold more athletes adhere to a GFD than clinically requiring gluten-avoidance.

Lis D, Stellingwerff T, Shing CM, Ahuja K, DK, Fell J. Exploring the popularity, experiences, and beliefs surrounding gluten-free diets in nonceliac athletes. Int. J. Sport Nutr. Exerc. Metab. 2015; 25:37-45.

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Food avoidance in athletes: FODMAP foods on the list. Appl. Physiol. Nutr. Metab. 2016;41(9):1002-4.

Study 2: Double blind crossover intervention investigating gluten-free diets on inflammation and performance in nonceliac athletes

7-Day GFD vs gluten-containing diet GCD (n=12; **Fig. 3**)

Measures

1. Exercise performance (45 min steady state @ 70%W_{max} + 15min TT)
2. Intestinal Injury
3. GI symptoms
4. Perceived wellbeing (Daily Analysis of Life Demands in Athletes (DALDA)
5. Systemic inflammation.

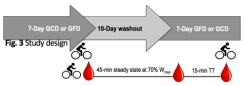

Fig. 3 Study design

- No significant different in GI symptoms (Fig. 4) or performance (Fig. 5) between a GCD and GFD.

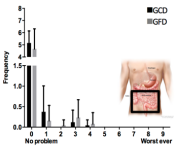

Fig. 4 Lower GI symptoms over 7-days of GCD vs GFD intervention.

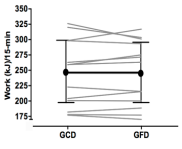

Fig. 5 15-min TT performance on day-7 of GCD vs GFD intervention.

No significant difference between a gluten-containing and GFD on: exercise performance, GI symptoms, overall wellbeing, markers of epithelial injury or systemic inflammation.

Lis D, Stellingwerff T, Kitic CM, Ahuja KD, Fell J. No effects of a short-term gluten-free diet on performance in non-celiac athletes. Med. Sci. Sports Exerc. 2015b;47(12):2563-70.

Study 3: Case Study-Low FODMAP diet intervention on GI outcomes and perceived wellbeing

In a healthy athlete with exercise-associated GI distress, (serology negative for CD, no functional GI disorders or food intolerance) a 6-day habitual high FODMAP diet was compared to low FODMAP dietary intervention **(Fig. 6)**. Food and exercise was replicated.

Measures

1. Daily GI symptoms and during exercise GI symptoms
2. Perceived wellbeing

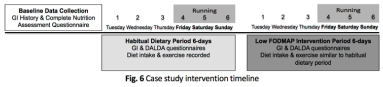

Fig. 6 Case study intervention timeline

- Daily GI symptom and during exercise and GI symptoms showed a measurable reduction with a short-term low FODMAP intervention **(Fig. 7)**.
- DALDA scores of "worse than normal" ranged from 3-10 (average 6.1) during the habitual diet compared to 0-8 (average 3.7) during the low FODMAP diet.

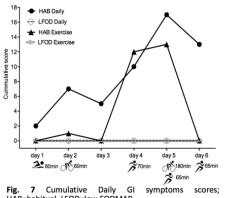

Fig. 7 Cumulative Daily GI symptoms scores; HAB=habitual, LFOD=low FODMAP.

A short-term low FODMAP intervention was effective in reducing GI symptoms for this GI symptom prone athlete; however, randomized-controlled trials are required to assess the suitability of low FODMAP diets for reducing GI distress in other symptomatic athletes.

Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Case Study: Utilizing a Low FODMAP Diet to Combat Exercise-Induced Gastrointestinal Symptoms. Int. J. Sport Nutr. Exerc. Metab. 2016;10.1123/ijsnem.2015-0293:1-17.

Appendix 4 – Gluten-free diet survey tool

Questionnaire to Assess the Popularity of Gluten Free Diets in Athletes Survey

1. I am an athlete competing in the following sport.
Cycling (track, mountain, road)
Triathlon and other multisport (all distance)
Ultra--endurance
Middle and Long Distance Running
Swimming
Rowing
Sprinting, Jumping & Throwing
Field-Based Team
Skill--based (curling, archery, shooting)
Court and Indoor Team
Racket
Strength and Power (Olympic lifting)
Weight-classed (wrestling, boxing)
Gymnastics
Figure and Speed Skating
Hockey and Ringette
Winter-ski
Winter-snowboard
Other (please specify)

2. What level of performance would you currently rank yourself?
Recreational/Active
Recreational Competitive (compete at high level)
Provincial/State (e.g. compete at provincial/state championships)
National (e.g. compete at National championships)
International (e.g. routinely compete as an invited athlete at international competitions or World Cups)
World or Olympic Qualifier + International Competitor
World or Olympic medalist + International Competitor
Professional Athlete (e.g. major league soccer)
Other (please specify)

3. What is your gender?
Female
Male

4. What age bracket do you fall into?
< 18
18-24
25-30
31-40
41-50
50+

5. What best describes your dietary intake habits with regards to your frequency of gluten free diet?
100% of the time
90-99% of the time
76-89% of the time
50-75% of the time
Sporadically (a few days a month or a few weeks here and there)
Buy gluten free products once in a while
Around competition time (1–2 weeks before)
Not at all
Other (please specify)
0% of the time

6. How often do you experience gastrointestinal issues during exercise?
(Gastrointestinal issues include but are not limited to bloating, diarrhea and gas).
1-5% of the time
6-5% of the time
16-25% of the time
26-35% of the time
36-50% of the time
> 50% of the time

7. Regardless of if you have in the past or currently follow a gluten free diet, what are your viewpoints about a gluten free diet (check all that apply)?
It is overall healthier
Reduces gastrointestinal distress (bloating, flatulence, diarrhea, constipation)
Reduces fatigue or improves energy
Reduces inflammation
Improves immune system function
Improves exercise performance
Improves recovery after exercise
Only applicable for people clinically diagnosed with celiac disease or gluten sensitivity people
Is not for me because I do not experience any of the related symptoms

8. Have you experienced any of the following symptoms that you associate with dietary intake (check all that apply)?
Abdominal bloating, gas, pain, cramping or distention
Unexplained weight loss/obesity
Chronic diarrhea (can be accompanied by constipation)
Pale, foul smelling stool (steatorrhea)
Anemia or other nutritional deficiencies
Irritability, anxiety, depression, fatigue
Bone or joint pain
Hypoglycemia
Muscle cramps, mouth sores, hair loss
Missed menstrual periods
Gluten ataxia (loss of full control of bodily movements)
Tingling or numbness in extremities
Bone density loss (osteoporosis/osteopenia)
Extremely itchy rash
Other (please specify)

9. If you answered YES to any of the above, what dietary components do you think these symptoms may have been caused by (check all that apply)?
Dairy (milk, cheese, yogurt…)
Excess fructose (apple, mango, honey…)
Fructans (asparagus, beet root, garlic, leeks…)
Fructose (apple sauce, pears, agave…)
Galactans (legumes, beans, lentils)
Gluten (wheat bread, bran flakes, whole wheat pasta…)
High fat or fried foods
Lactose (milk, ice cream, custard, soft cheese…)
Polyols (apricot, cauliflower, sorbitol…)
Very high fiber foods (brussel sprouts, broccoli, bran flakes…)
Don't know
Other (please specify)

10. Have you tried eliminating any of the dietary components you have checked off in question 9?
Yes
No

11. Has removing the dietary components indicated in question 9 reduced symptoms you have in indicated in question 8?
Yes
No
I have not removed for long enough to notice a difference

12. What other dietary changes do you think may take place consciously or unconsciously with the elimination of gluten (check all that apply)?
More conscientious overall nutrition intake
Less processed foods
Less sugary foods
More fruit and vegetables
More gluten free whole grains
More balanced meals
None
Other (please specify

13. What other physiological changes do you think may take place consciously or unconsciously with the elimination of gluten (check all that apply)?
Improved exercise performance
Decrease inflammation
Decreased illness
Better body composition
Better training adaptations
Less fatigue from training
Decreased fatigue on a daily basis
Less muscle stiffness, soreness
Less gastrointestinal issues (i.e. boating) during exercise
Other (please specify)

14. Do you believe that removing gluten from the diet improves exercise performance (e.g. sprint faster, run longer, cycle at high power output)?
Yes
No
Not sure

15. What best describes any basis you have been given for a gluten free diet.
Clinically diagnosed with gluten sensitivity by physician using a gluten free challenge test
Clinically diagnosed with Irritable Bowel Syndrome (IBS)/similar condition that is made worse with gluten.
Clinically diagnosed wheat allergy
Self--diagnoses based on symptoms
Family history of celiac disease
Naturopath diagnosis based on bloodwork
No identifiable symptoms, but decided to follow gluten free diet
I have been told eating gluten free diet is good, but have not tried it yet.
None, I have not been told anything about a gluten free diet.
Other (please explain)

16. What best describes the advice you were given about a gluten free diet?
Follow a gluten free diet all the time
Follow a gluten free diet before and during competition
Follow a gluten free diet as much as you can
Try a gluten free diet and see if it help with performance and symptoms
None, I have not been given advice on a gluten free diet
Other (please specify)

17. Where have you accessed information about gluten free diets and athletic performance (check all that apply)?
Online forums
Celiac or gluten intolerance information websites
Academic journals
Registered Dietitian
Nutritionist
Trainer
Coach
Naturopath
Other athletes
I have not read any information
Other (please specify)

Appendix 5 – GI symptom questionnaires

DAILY GI QUESTIONAIRRE

Participant #: **Date:** **Time:**

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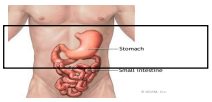
***Complete this at the end of the day**

Were you on your menstrual cycle today? ☐ yes ☐ no ☐ N/A

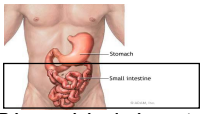
GI problems DURING THE DAY outside of training

Please rate if you experienced any of the following symptoms **DURING THE DAY:**



A Upper abdominal symptoms	no problem at all **0**	Very, very minor problems **1**	very minor problems **2**	minor problems **3**	moderate problems **4**	serious problems **5**	severe **6**	very severe **7**	Very, very severe **8**	the worst it has ever been **9**
Reflux	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Heartburn	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Burping	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Bloating	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Stomach pain / cramps	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Vomiting	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nausea	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

What time? How long?



B Lower abdominal symptoms	no problem at all **0**	Very, very minor problems **1**	very minor problems **2**	minor problems **3**	moderate problems **4**	serious problems **5**	severe **6**	very severe **7**	Very, very severe **8**	the worst it has ever been **9**
Flatulence	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Urge to defecate	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Left abdominal pain (cramp)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Right abdominal pain (cramp)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Loose Stool	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Diarrhoea	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Intestinal Bleeding	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

What time? How long?

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Modified from Beate Pfeiffer • University Birmingham

1